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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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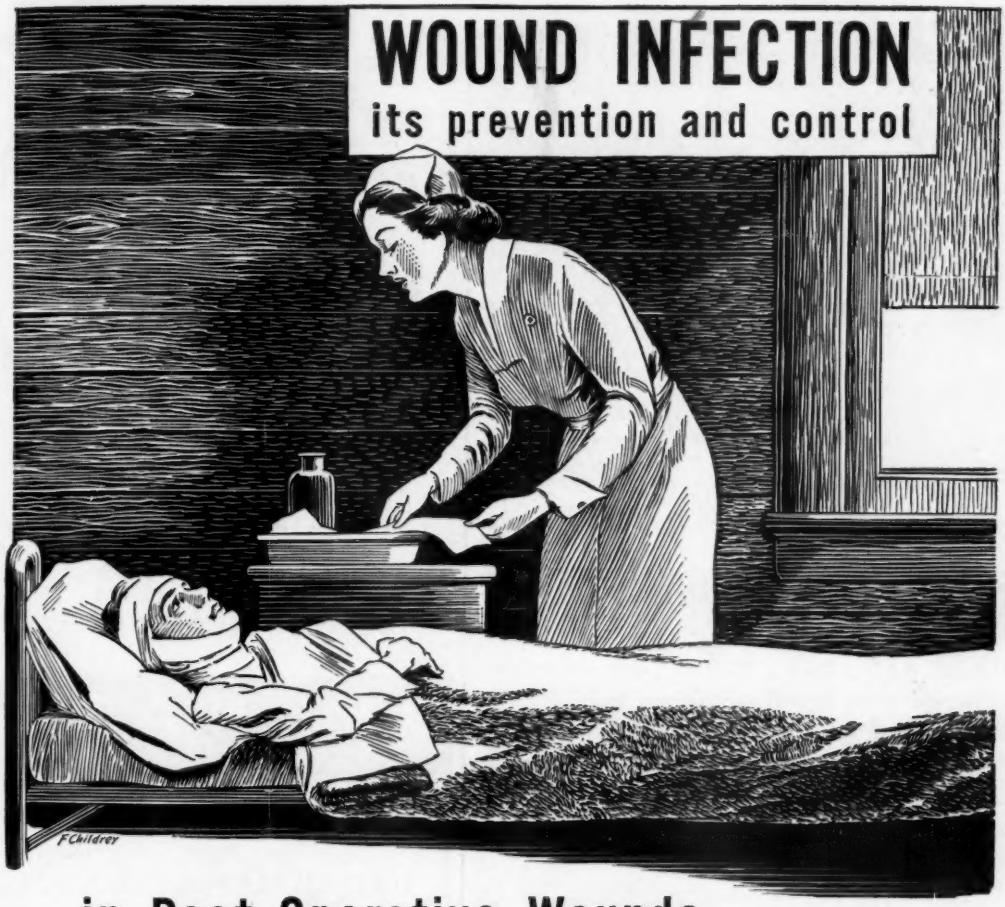

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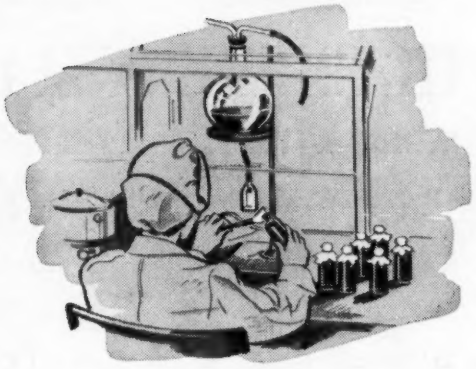

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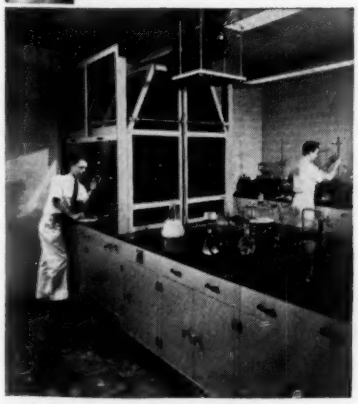

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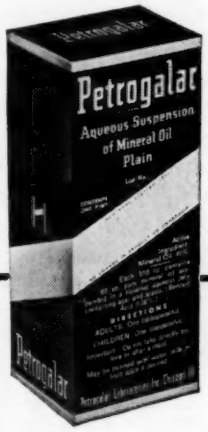

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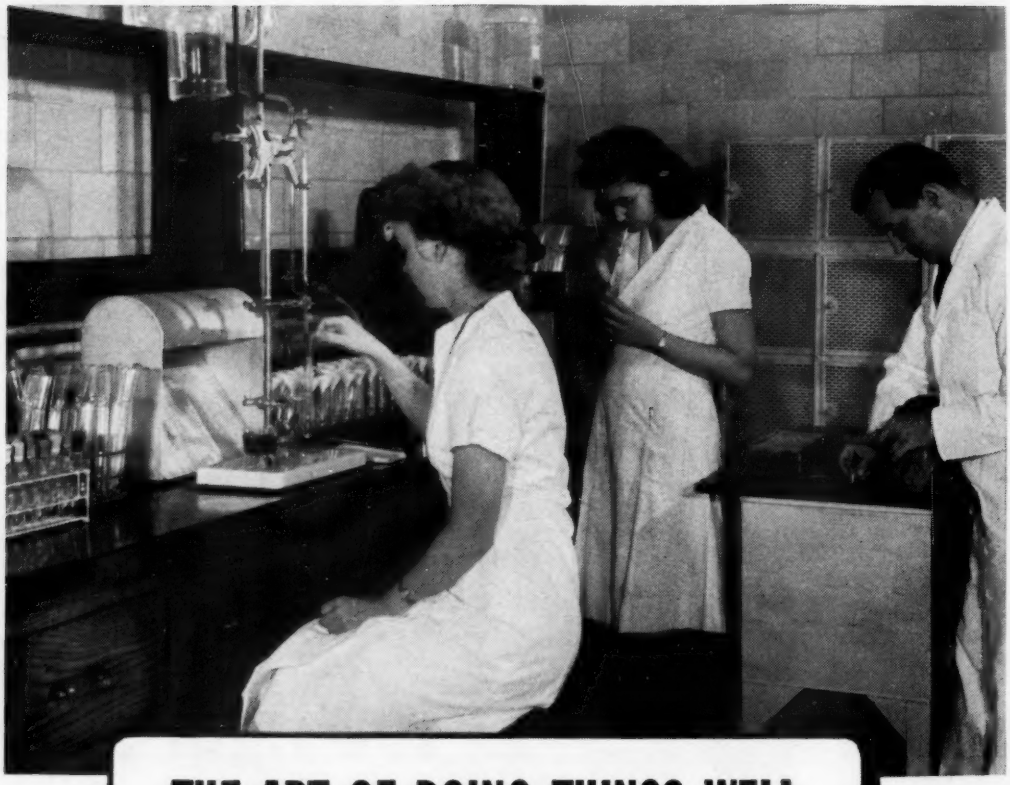

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SURGERY

VOL. 12 OCTOBER, 1942 NO. 4

Original Communications

INTERNAL WIRING FIXATION OF FACIAL FRACTURES

WILLIAM MILTON ADAMS, M.D., MEMPHIS, TENN.

DUE to the increased number of extensive facial fractures within the last few years, there is an obvious need for a method of treatment of such fractures which may be quickly applied and one which affords complete immobilization. After using numerous types of extraoral appliances, including those attached to plaster headcaps, for immobilizing fractures of the maxilla and other facial bones, the author has found these appliances are complicated, their preparation and application are time consuming, they are cumbersome and uncomfortable for the patient, and they require close watching and repeated adjustments on the part of the surgeon. The fact that practically everyone treating these fractures has a different type of extraoral appliance suggests that this method is not entirely satisfactory.

During the past eight years, we have treated eighty-five fractures of the maxilla. The occurrence of head and other facial injuries with fractures of the maxilla is shown in Table I.

As may be seen, there were three fatalities in this series, all three of the patients having had an associated brain injury. Two died of concussion and contusion of the brain, and the third of cerebral meningitis. All expired before their physical condition would permit manipulative procedures for reduction of the facial fractures.

Until two years ago, some type of extraoral appliance was generally employed in these cases. Since then, open reduction and fixation by wiring of the fractured parts to the neighboring unfractured bony structures have been carried out in all cases wherein immobilization was required, with three exceptions; in these three, open reduction was contraindicated and it was necessary to resort to the use of an extraoral appliance.

Received for publication, May 22, 1942.

This method not only meets the requirements of facility of operation, complete immobilization, and sound surgical principles, but is applicable to practically every type of fracture of the facial bones. The procedure may be carried out with only a pair of pliers, a small drill and dissecting set, and a spool of fine stainless steel wire. Since complete immobilization is obtained, repeated adjustments are unnecessary and the patient is spared much discomfort and inconvenience. Patients are usually able to resume their activities after the tissues have recovered from the acute stage of the injury and when healing is complete the wires are easily removed. Regardless of how extensive the fractures, immobilization by this method has proved far simpler and more satisfactory than by the use of extraoral appliances attached to plaster headcaps.

TABLE I

DISTRIBUTION OF EIGHTY-FIVE FRACTURES OF THE MAXILLA AND ASSOCIATED INJURIES (1934 TO 1941)

YEAR	NUMBER OF CASES	FRACTURE OF THE MANDIBLE	FRACTURE OF THE ZYGOMA	FRACTURE OF THE NASAL BONES	FRACTURE OF THE SKULL	FACIAL LACERATIONS	INFECTION WITH DRAINAGE	DEATHS
1934	4	1				3		
1935	8	3	3		1	6		1
1936	5	1	3	1		3		
1937	4	1	3	1	1	1		
1938	12	2	3	3		9	1	
1939	13	2	3	3	1	10		1
1940	17	2	2	4	1	11	2	1
1941	22	7	5	4	1	17	2	
Total	85	19	22	16	5	50	5	3

Undoubtedly, in the exceptional case, extraoral appliances are essential and therefore should be included in the armamentarium of every surgeon who does this type of work. In the presence of infection, particularly in compound fractures, open reduction is definitely contraindicated. Even here, however, an extraoral appliance may be required only for temporary immobilization; after the infection subsides, one may remove the appliance and wire the fragments together.

The treatment of fractures of the facial bones must, of course, be individualized. In greenstick fractures of the maxilla with only slight malocclusion of the teeth, for example, immobilization by open reduction or extraoral appliances may not be necessary. Motion of the lower jaw against the upper will generally shift the teeth into occlusion.

Diagnosis.—In acute injuries of the face, the surgeon should have no difficulty in recognizing gross fractures of the facial bones, even without roentgenograms. Although roentgenograms afford valuable information and should be made in all cases as soon as the condition of the patient permits, as a rule, an accurate diagnosis may be made by careful inspection and palpation. Examination by palpation should be

carried out on both sides at the same time, with special attention to any asymmetry, irregularities, or crepitus.

In fractures of the maxilla with downward displacement, inspection will reveal an elongation of the middle third of the face; if the maxilla has been depressed backward as well, the patient will have a "dish-pan" face, particularly if the nasal bones are also depressed, and the teeth will be in malocclusion.

In any facial injury, one should always determine whether the upper jaw is movable. This is easily accomplished by grasping the upper teeth between the fingers of one hand while supporting the back of the head with the other. Motion may be up and down or from side to side. When up and down, movement of the infraorbital ridges may often be detected. One should also observe whether motion of the lower jaw is limited on opening and closing or in the shift from side to side.

Roentgenograms should be made routinely in the posterior-anterior and lateral views, and should include all the facial bones of both the upper and lower jaws. Some fractures, especially those of the temporomandibular joint, may not be demonstrated in these routine films; when such fractures are suspected, roentgenograms in special views should be made.

Anesthesia.—If the bony fragments are not impacted and reduction is possible by manipulation, the procedure may be carried out under local anesthesia. In more difficult cases a general anesthetic is necessary, the type depending largely upon the skill of the anesthetist. Intratracheal anesthesia and sodium pentothal are both satisfactory, but should be given only by one well-trained in their administration. When there is any doubt as to the choice of the anesthetic, the use of ether by the open method is advisable.

Technique.—After the diagnosis has been made, one should visualize the fractured parts in their architectural relationship to the normal bony structures, without regard to the overlying soft tissues. The treatment then should be relatively simple. The soft tissue wounds should, of course, be treated in the usual manner.

Fractures of the maxilla are rarely encountered alone, rather, they are generally associated with fractures of one or more of the other facial bones, including the mandible. Since the maxilla is the foundation structure, accurate apposition and immobilization of this fracture is of prime importance; once these are accomplished, immobilization of the secondary fracture offers little difficulty.

In carrying out this method of open reduction and fixation of fractures of the facial bones, it is necessary to make an incision at only one or two sites: overlying the infraorbital ridge, or at the lateral margin of the supraorbital ridge, depending upon the bones involved. In the event of a laceration over either of these areas, the wires may be inserted through the wound.

In a simple bilateral fracture of the maxilla (Fig. 1), a small incision is made over the infraorbital ridge on either side. A hole of sufficient size to accommodate a No. 25 or 26 stainless steel wire is bored through the infraorbital ridge. The wire is then threaded through the opening, looped over the ridge, and both ends are passed together along the anterior wall of the antrum into the upper sulcus over the second molar teeth, where they are caught with a hemostat. One is surprised at the ease with which the wires are directed to the desired point of exit without the use of a guide. The fractured bone is then elevated to its normal position and the wires are drawn taut and fixed to one or more of the teeth. The use of the loop around the infraorbital ridge is much more simple than tying the wire and its subsequent removal is easily accomplished.

If the patient is edentulous, the wires may be attached to the false plate, provided it is intact; otherwise, dental wax may be molded around the alveolar ridge and over the hard palate, the wires drawn across the palate and tied in the midline, and the ends imbedded in the wax.

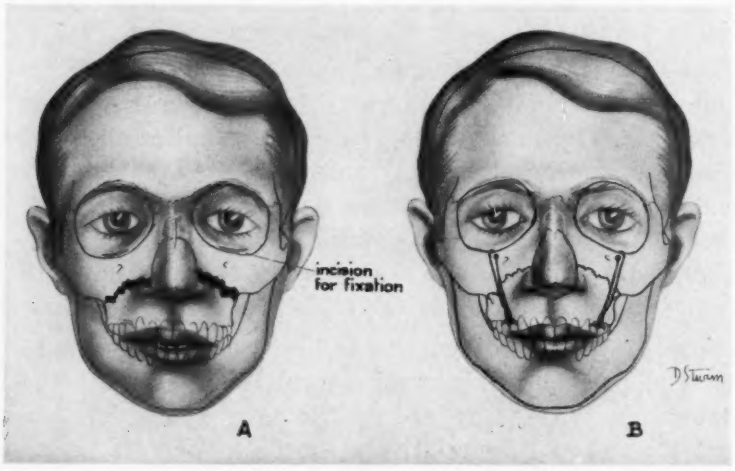

Fig. 1.—*A*, Complete bilateral horizontal fracture of maxilla; *B*, maxilla elevated and maintained in normal position with wires extending from the infraorbital ridges to the upper teeth.

Once the wires enter the contaminated field of the mouth, they should not be drawn upward through the soft tissues. If removal is necessary, the loop should be cut and the wires withdrawn from below.

In fractures of the maxilla associated with comminuted fractures of the infraorbital ridge (Fig. 2), it is sometimes necessary to immobilize the major fragment of the ridge to the outer half. This may be done through the same soft tissue incision. An additional hole is drilled through the medial fragment and a small loop of wire is inserted through the two holes and tied. The smaller fragments, after restoration to their normal position, will usually remain in place, being sup-

ported by the immobilized large fragment. Following wiring fixation of the infraorbital ridge, intra-antral packing with gauze or other substance is unnecessary.

Should the maxilla be separated in the midline, the teeth on the fractured side are fixed to those of the sound side. In many cases a simple loop of wire is sufficient, though in more complicated cases, with loss of the teeth, an arch band may be required (Fig. 3).

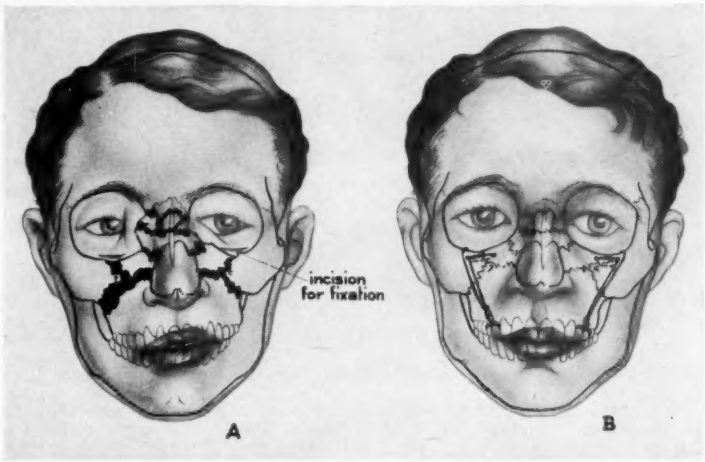

Fig. 2.—*A*, Complete bilateral fracture of maxilla with comminuted fractures of nasal bones and infraorbital ridges. *B*, Maxilla held in position by wires from the malar bones to the upper teeth; lower fragments of infraorbital ridges immobilized by separate wiring; fixation not necessary for smaller fragments.

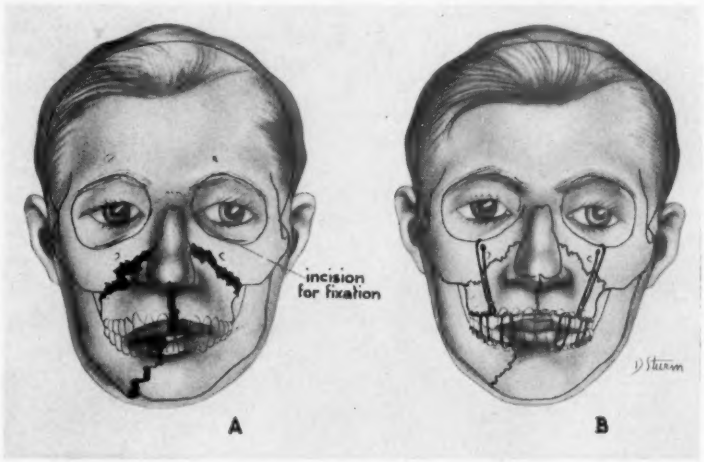

Fig. 3.—*A*, Complete bilateral fracture of maxilla with separation in midline; associated compound fracture of the mandible at the symphysis. *B*, Metal arch bands attached to upper and lower teeth, fractures of maxilla reduced and held in normal position with wires from infraorbital ridges to upper arch bands on both sides; upper and lower teeth fixed in occlusion with orthodontic rubber bands.

For reduction and immobilization of fractures of the maxilla with associated fractures of the zygoma or malar process (Fig. 4), an incision is made over the ridge of the frontal bone lateral to the supra-

orbital rim, just above the zygomatic-frontal suture line. With an elevator, the periosteum is separated from the frontal bone and a small hole is drilled through the ridge. A wire is threaded through the opening, looped over the ridge, and the two ends are passed beneath the

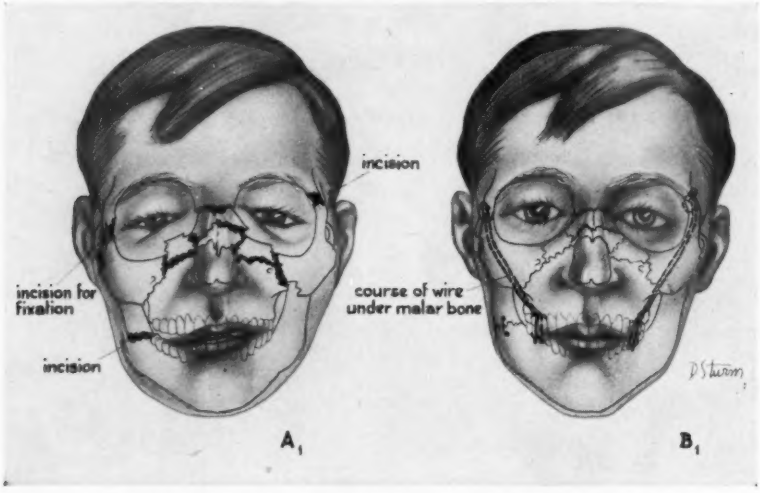

Fig. 4 (Case 1).—A_1, Complete bilateral fracture of maxilla, comminuted fracture of infraorbital ridges, and nasal wings, fracture of both malar bones; fracture of right mandible just above angle of jaw. B_1, Fracture of right malar bone reduced and wire passed from frontal bone behind body of malar bone and attached to upper teeth, fixing the maxilla and malar bones on this side. Same procedure repeated on left, and, in addition, malar wired separately to frontal bone because of gross displacement; fracture of right angle of mandible fixed by open reduction and wiring, upper and lower teeth wired in occlusion.

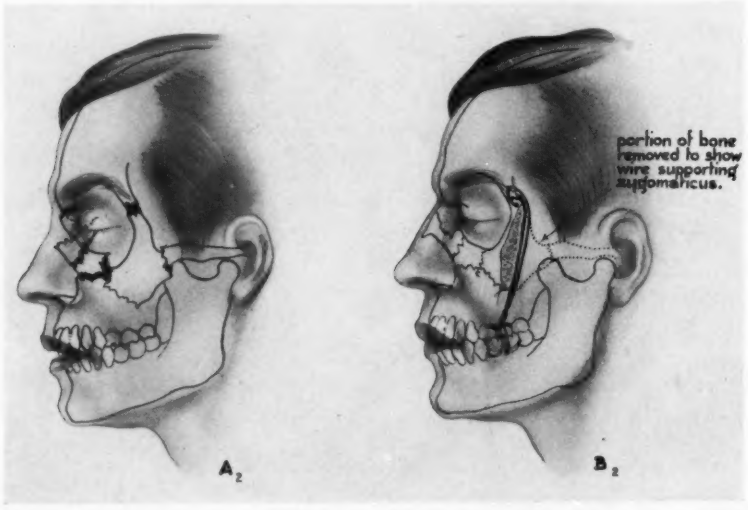

Fig. 5 (Case 1).—A_2, Lateral view, left side, showing fractures of the facial bones; B_2, lateral view, showing course of wire from the frontal bone to the upper teeth, supporting the malar bone in normal outward and upward position.

temporal surface of the malar bone, making their exit in the upper sulcus in the region of the first or second molar. The displaced bones are elevated to their proper positions and the wires are tied to the

teeth, exerting an upward and outward pull on the malar bone, holding it up in normal position. Should there be any question as to the adequacy of fixation, one should not hesitate to drill another hole in the malar bone just below the zygomatic-frontal suture line and, with a small loop of wire, fix the malar bone to the zygomatic process of the frontal bone (Fig. 5, B_2).

In these cases, the malar bone and zygomatic process may be elevated by several other methods. By such methods, however, the malar bone, if completely detached, may subsequently be displaced by the strong pull of the masseter muscle. With the procedure described, the bones may easily be restored to their normal positions and the malar bone firmly fixed to the frontal bone by wiring, through the one incision. Associated fracture of the zygomatic arch, after reduction, does not require fixation, since it has adequate support from the underlying temporal muscle.

Following reduction and immobilization of fractures of the maxilla and other facial bones, associated fractures of the nasal bones are reduced and maintained in position by a nasal splint, according to the routine method of treating such fractures when encountered alone.

In bilateral fractures of the facial bones, the foregoing procedures are carried out, as indicated, on both sides. In bilateral horizontal fractures of the maxilla with separation in the midline (Fig. 3), the two halves are drawn together and immobilized with arch bands or wires. This should precede open reduction and fixation of the maxilla to the upper unfractured bones. If the mandible is not fractured, fixation of the upper to the lower jaw is unnecessary.

Oral Hygiene.—This is of the utmost importance. The mouth should be thoroughly irrigated every hour until the infectious stage has passed, and thereafter three or four times daily. Normal saline, boric acid, or any mild antiseptic solution may be used for the irrigations, though ordinary tap water suffices. Sterile solutions are neither practicable nor necessary. Unless quite sick, the patient may himself carry out the procedure. The equipment consists merely of a large douche can or intravenous flask and three feet of rubber tubing to which a hard rubber or metal irrigating tip is attached. The can is placed at least two feet above the patient's head, so that the force of the stream may be ample to insure adequate cleansing. In addition to this measure, the patient should be encouraged to brush his teeth with a small brush when possible.

The wires are allowed to remain in place for three to nine weeks, depending upon the location and type of the fracture. One may feel free to leave them undisturbed as long as necessary, since they cause little or no discomfort, as in the case when an extraoral appliance is used.

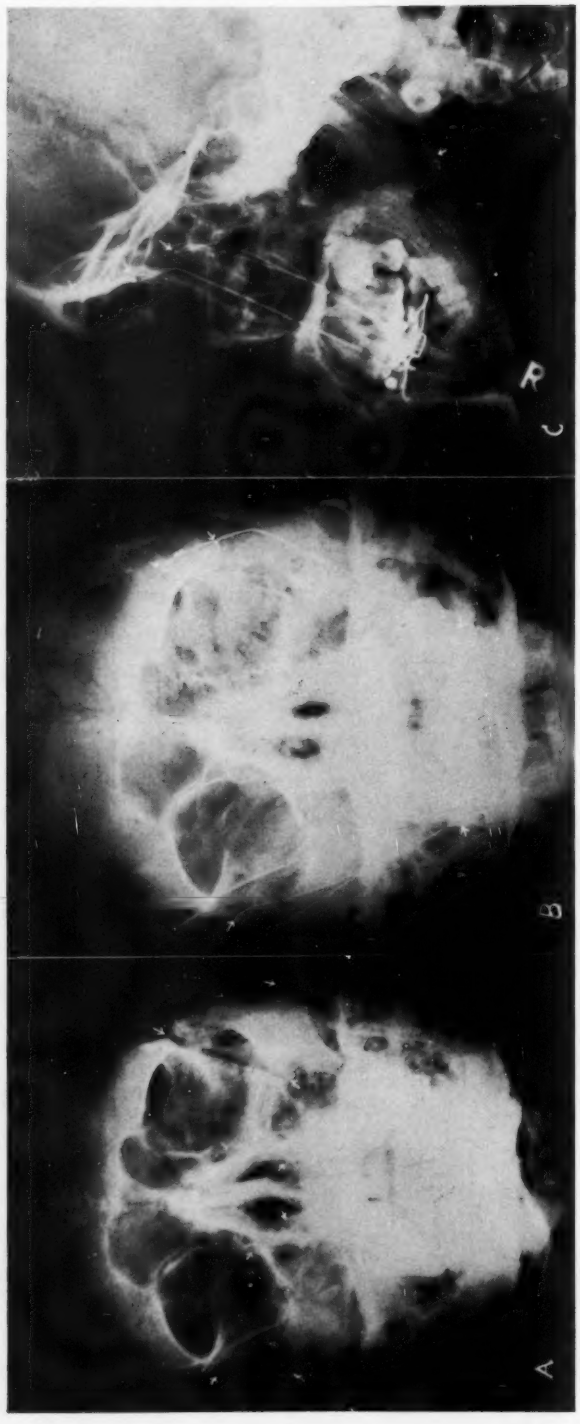

Fig. 6 (Case 1).—*A*, Preoperative roentgenogram, arrows designating fractures; *B* and *C*, roentgenograms after open reduction and fixation, points of wiring designated by arrows.

After healing is complete, the wire is severed through a small spear-point incision over the loop and removed through the mouth, in order to avoid contamination of the soft tissues above.

Nature is kind in the treatment of these facial injuries, in that the blood supply of the tissues is abundant and healing takes place quickly. The scar over the infraorbital ridge, being horizontal, is almost invisible, while that over the supraorbital ridge is at the edge of the eyebrow and consequently is also inconspicuous.

In only one case treated by the above method has infection developed. This was a bilateral fracture of the maxilla with fractures of both zygomas and of the nasal bones. Paradoxically, it was the first case in which we ever used sulfanilamide locally. The drug was placed in the wound on only one side, and this was the wound which became infected. The wires were not disturbed, as the infection subsided following incision and drainage and treatment with hot compresses. There was no infection in the wound of the opposite side wherein sulfanilamide was not used.

The following cases illustrate the application of this procedure in the various types of fractures of the facial bones.

CASE 1.—W. W., a white male, aged 52 years, was lying on the floor, working on the rear axle of a car from which the wheels had been removed, when the jacks slipped and the axle fell across his face. He was admitted to the hospital four hours later, suffering acutely and in a state of mild shock. Pantopon was given and the routine treatment for shock, including glucose intravenously, was carried out.

On inspection, all the soft tissues of the face were grossly swollen, the eyelids being almost completely closed from the edema. The middle third of the face was elongated from displacement of the maxilla inferiorly and posteriorly, the orbital rim was elongated vertically from a downward displacement of the infraorbital ridges, there was a comminuted fracture of the nasal bones, and the malar bones were depressed. On palpation, it was apparent that all the facial bones were crushed. In addition, there was a fracture of the mandible just above the angle on the right, with anterior and lateral displacement of the posterior fragment.

Almost immediately following the emergency treatment, the patient had a severe rigor, followed by a temperature of 104° F., and it was felt unwise to manipulate the fractures at this time. His fever subsided under treatment with sulfanilamide and two days later reduction and immobilization were carried out under local anesthesia.

The left malar bone was widely displaced, necessitating separate wiring to the zygomatic process of the adjacent frontal bone. Small holes were then drilled in the frontal bone lateral to the orbital region just above the zygomatic-frontal suture line on both sides, a No. 25 stainless steel wire was threaded through the opening, and the two ends of the wire were carried downward behind the malar bone and under the soft structures of the cheek, into the upper sulcus of the mouth in the region of the first and second molars. After elevation of the zygomatic arches and malar bone, the soft tissue wounds were closed. Eyelet wires were next placed around the upper and lower molar teeth on both sides. The maxilla was then restored to its normal position and the wires from above were drawn taut and tied to those about the teeth of the lower jaw. In this manner the teeth were held in occlusion and, at the same time, the fractured bones were maintained

Fig. 7 (Case 1).—*A*, Preoperative photograph two days after injury; the displacement of the facial bones is obscured by the swelling of the overlying soft structures. Due to the downward displacement of the maxilla, the patient was unable to bring teeth of the lower jaw in occlusion with the upper jaw. *B*, and *C*, Two months postoperative, showing teeth in occlusion and normal facial contour.

in proper position. The anterior wall of the antrum was elevated with a male urethral sound inserted through the nares, the nasal bones were replaced, the passages packed with vaseline gauze, and an external nasal splint was applied.

Postoperative roentgenograms revealed the maxilla and other facial bones in good position. The displacement at the right angle of the mandible, however, was still apparent. Since it was impossible to reduce and maintain this fracture in normal position by manipulation, an incision 2 cm. long was made over the angle and the bones were apposed and fixed with a No. 25 stainless steel wire.

During the first week, oral irrigations were carried out hourly, supplemented by the use of oral pentacresol at frequent intervals. The patient had a slight temperature for several days, though this gradually subsided under treatment with sulfanilamide. He improved rapidly thereafter and was able to leave the hospital two weeks following his admission. The wires around the facial bones were removed in the office eight weeks postoperatively. Because of the fracture of the mandible, it was necessary to maintain fixation of the lower to the upper jaw for a longer period. The patient now has full motion in the lower jaw, both vertically and laterally, the teeth are in good occlusion, and the contour of the face is normal.

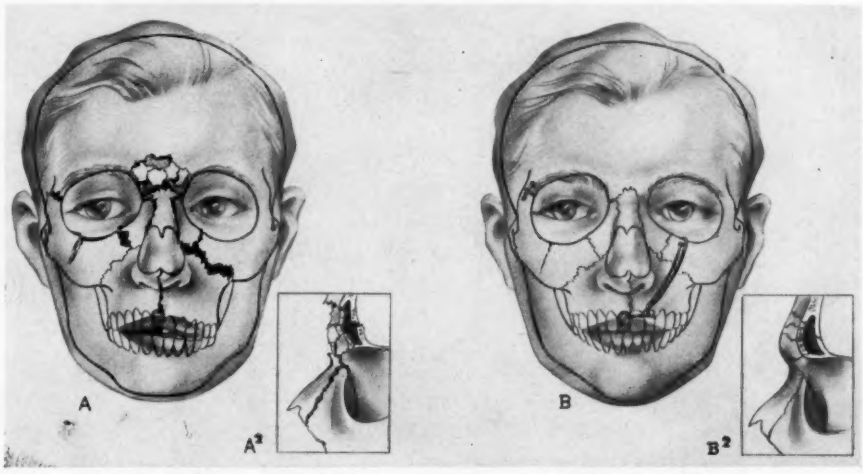

Fig. 8 (Case 2).—*A*, Bilateral fracture of the maxilla, greenstick fracture of the right half, without displacement; complete bony detachment of the left half of the maxilla with downward displacement of the right malar bone, crushing fracture of the nasal bones and infraorbital ridges, depressed fracture of the anterior and posterior walls of the frontal sinus, fracture of the cribriform plate.

B, After reduction of fractures, the points of wiring fixation at the right zygomatico-frontal suture line and the left infraorbital ridge.

A_2, Lateral view showing fractures of the frontal sinus region. B_2, postoperative lateral view.

Case 2.—H. A. was a white male, aged 33 years. He was a passenger on the front seat of a car which was driven into a telephone pole, causing the mid-portion of his face to strike the instrument board. He was admitted to the hospital an hour later and immediately given routine treatment for shock.

There was a laceration two inches long through the periosteum of the forehead; multiple lacerations about the right eye; a deep stab wound over the upper part of the nose and frontal sinus region, extending into the frontal sinus and nasal cavity; lacerations of the right ala; and an irregular through-and-through laceration of the upper lip. The middle part of the face was depressed and elongated. The right upper central and lateral incisors had been knocked out, and the remaining upper, as well as the lower central incisors were loose.

Fig. 9 (Case 2).—*A* and *B*, Preoperative roentgenograms; arrows designate fractures. *C*, Immediate postoperative roentgenogram showing facial bones after wiring fixation. *D*, Postoperative roentgenogram one year later; the wire at the right frontozygomatic suture line still in place, facial bones in satisfactory position.

Examination revealed a compound crushing fracture of the nasal bones extending into the frontal sinus; the anterior wall of the frontal sinus was depressed and in contact with the posterior wall, and there was an opening in the posterior

Fig. 10 (Case 2).—*A*, Photograph immediately after injury showing multiple lacerations and distortion of facial features; downward displacement of the right eye. *B* and *C*, Postoperative photograph one year later showing perfect occlusion of the teeth with satisfactory restoration of normal facial contour.

plate through which a small amount of brain tissue protruded. All the bony structures of this region were movable, including the cribriform plate. In addition, the infraorbital regions were crushed inward, there was a greenstick fracture

of the right maxilla without displacement, a fracture of the left half with gross downward and backward displacement, complete detachment of the right malar bone, and a depressed fracture of the zygomatic arch.

The skin about the wounds was thoroughly cleansed, local anesthetic given, and the wounds copiously irrigated with warm saline solution. Through one of the soft tissue wounds at the outer margin of the supraorbital ridge on the right, the fracture in the frontozygomatic region was exposed and with a heavy metal elevator and external manipulation, the malar bone and zygomatic arch were restored to normal position. The malar bone was anchored to the zygomatic process of the frontal bone with small stainless steel wire and the incision was closed.

Before manipulation of the fractures about the nose and maxilla, the nasal mucosa was cocainized and the maxillary region was anesthetized with nerve block and deep infiltration of novocain. Through a small incision over the left infraorbital ridge, a hole was then drilled in the unfractured portion of the left malar bone and a loop of wire threaded through the opening and passed down beneath the soft tissues of the cheek along the anterior wall of the antrum, into the upper sulcus. The fracture of the maxilla was next reduced, the occlusion of the teeth tested by bringing the lower jaw into contact with the upper and the wire tied around the upper teeth on the left side, holding the maxilla up in proper position.

Because of the fracture of the cribriform plate, extreme care was exercised in reducing the fractures about the nose and frontal sinus region. The anterior wall of the frontal sinus was elevated and the sinus again copiously flushed with normal saline solution. Since there was a large fracture opening from the frontal sinus to the nasal cavity, the overlying soft tissue wound was closed without external drainage.

After replacing the bony cartilagenous nasal septum in the midline, a small stainless steel wire was threaded through and through the nose over a lead plate on each side. With a trocar antral windows were then made under the inferior turbinates. In order to allow free drainage, packing of the nasal passages was omitted. The patient left the operating room in fairly good condition, though the prognosis was regarded as poor.

An examination by a neurosurgeon revealed nothing of particular significance except the presence of blood from the middle ear in the external auditory canal on the left. Only conservative treatment was therefore advised.

The patient was given 15 gr. of sulfanilamide every four hours and fluids were limited. His temperature reached its highest of 102⅕° F. on the first postoperative day, and thereafter gradually subsided, reaching normal on the fifth day. The nasal splints were removed at the end of the week and he left the hospital three days later. His subsequent course was smooth, his only complaints being a double vision and vertigo. The fixation wire of the maxilla was removed in the office nine weeks after insertion.

It has now been two years since the injury and the patient has been working regularly for the past year and one-half. His facial contour is normal, occlusion of the teeth is perfect, the nasal passages are unobstructed, his hearing is not appreciably impaired, and he no longer has double vision. On turning his head quickly from side to side, he has a transient vertigo as a result of the injury to the left semicircular canal, but otherwise has no noticeable difficulty from the injury.

CASE 3.—T. S., a colored male, had been struck in the face by a train one hour before his admission to the hospital. In addition to multiple small lacerations about the face, he had a complete laceration of the upper lip in the midline, and a traumatic cleft extending through the alveolar ridge, the hard palate, and the nasal cavity, into the left antrum. The lower lip and tissues over the mandible were also completely lacerated in the midline and the symphysis was widely sepa-

rated. The two upper central incisors and the left lateral incisor were loose, and the lower central incisors had been knocked out. There was also a fracture of the zygomatic process on the right.

Roentgenograms demonstrated a greenstick fracture of the right maxilla without gross displacement, complete displacement of the right malar bone downward and inward with a fracture of the right zygomatic arch, a complete fracture of the left maxilla with the bone attached only to the soft tissues, detachment of the nasal bones from the frontal process with displacement to the right and downward, a crushing fracture of both infraorbital ridges downward, a midline fracture of the alveolar process extending into the hard palate with separation of the two halves, and a fracture of the mandible through the symphysis with wide separation.

Fig. 11 (Case 3).—*A*, Bilateral fracture of maxilla, greenstick fracture of right half and complete detachment of left half, with separation in the midline; fracture of both infraorbital ridges, dislocation of right malar bone, and compound fracture of the mandible at the symphysis.

B, Arch bands wired to upper and lower teeth, left half of maxilla immobilized in proper position with wires extending from body of malar bone to left upper teeth; fracture parts of infraorbital ridges wired together and right malar bone held in position by wire through frontal bone. Fixation of greenstick fracture of right maxilla was unnecessary; upper and lower teeth were maintained in occlusion with orthodontic rubber bands.

The soft tissue wounds were repaired immediately after the patient's admission to the hospital, but because of his poor condition, no attempt was made to treat the bony injuries. He ran a low-grade temperature for a few days, during which time sulfathiazole was administered. As soon as his general and local condition permitted, arch bands were placed around the upper and lower teeth to bring together the midline fractures of the maxilla and mandible. The bones were then restored to their normal positions and the fractures of the infraorbital ridges were immobilized by separate wiring of the fractured parts to the malar bone on both sides. To maintain reduction of the left maxilla, a wire was looped through the maxillary process of the malar bone and the ends brought down and attached to the arch band about the teeth. The right malar bone was wired to the frontal bone at the suture line. Although there was slight motion of the right half of the maxilla, being a greenstick fracture without displacement, wiring fixation was unnecessary. The teeth of the upper and lower jaws were brought into occlusion and held in place with rubber bands between the arch wires.

The arch bands and wire supporting the left half of the maxilla were removed six weeks later. The patient had no postoperative complications, and the roentgenograms showed all the fractured parts in good position.

Fig. 12 (Case 3).—*A*, Arrows designate fractures, as illustrated in Fig. 11, *B* and *C*. Roentgenograms after open reduction and internal wiring; points of fixation designated by arrows.

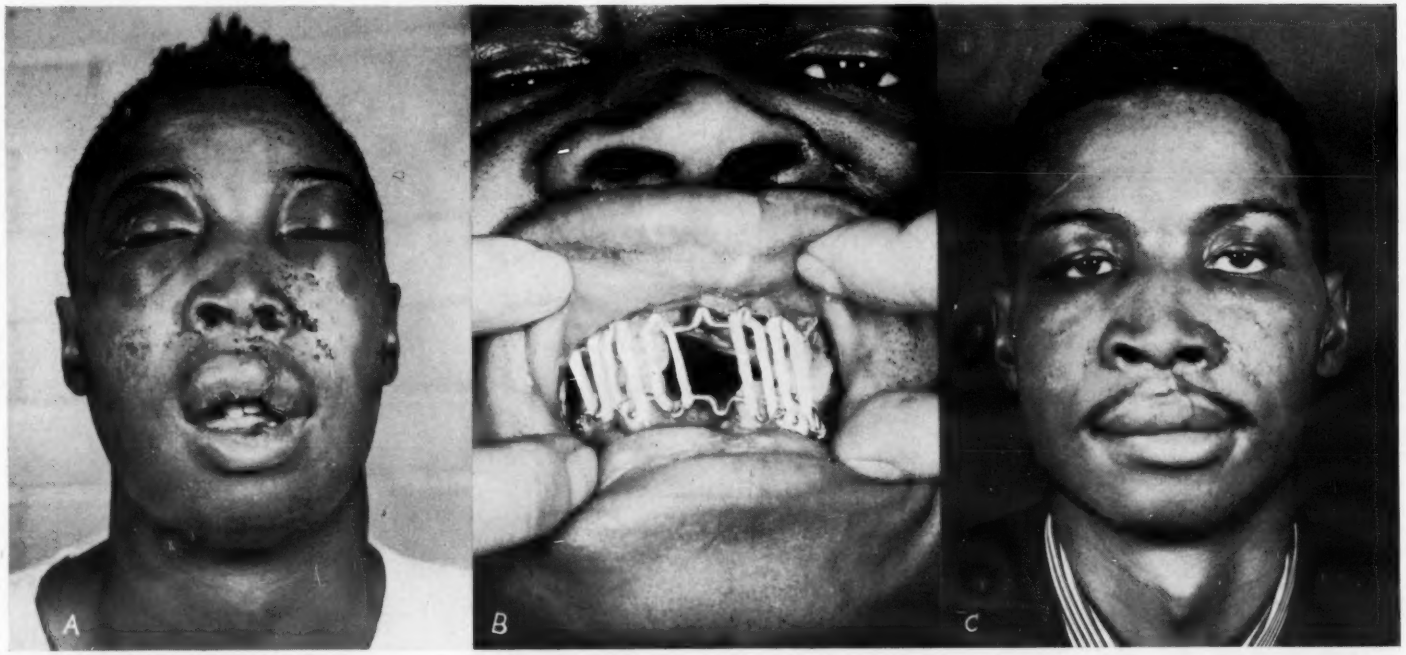

Fig. 13 (Case 3).—*A.* Preoperative picture one week after injury showing soft tissues still swollen, obscuring the deformity of the fracture and definite elongation of the middle one-third of the face; patient unable to bring teeth in occlusion.

B. Postoperative photograph showing arch bands around upper and lower teeth held together with orthodontic rubber bands.

C. Postoperative photograph two months later showing normal facial contour; scar of the upper lip may be improved by plastic repair.

SUMMARY

A simplified method of reduction and fixation of fractures of the maxilla and other facial bones has been described. For the approach, two small incisions are used at the outer or inferior orbital ridge, on one or two sides depending upon whether the involvement is unilateral or bilateral. The procedure requires a minimum amount of time and equipment, a small drill, pair of pliers, spool of small stainless steel wire, and a dissecting set.

THE BRONCHIAL FACTOR IN PULMONARY EMBOLISM

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IN PREVIOUS reports from this clinic, the reflex effects of pulmonary embolism on the heart[1] and on the pulmonary arterial tree[2] have been discussed. In this report we are presenting data concerning the behavior of the bronchial tree of the dog when pulmonary embolism is produced.

METHODS OF EXPERIMENTATION

Dogs weighing from 10 to 15 kg. were used. To visualize the bronchial tree, from 5 to 6 c.c. of iodochloral were injected with an 18 gauge needle directly into the trachea. The dogs were in a straight lateral position, with the head elevated from six to eight inches. The injection was made slowly, taking two and one-half minutes. After the injection had been completed, the animal's head was lowered to a horizontal position. For anesthesia, 0.3 c.c. of dial was injected per kilogram weight. The first film was taken five minutes after the injection was completed. The x-ray data were: the distance of the tube 29 inches, 30 Ma. with 70 to 75 kv. Exposure was 0.1 seconds. These factors were kept constant during the entire series.

The embolus was produced, as in our previous experiments from this laboratory,[1, 2] by injecting a mixture of barium sulfate, iron perchloride and normal salt solution, equal parts, into the femoral vein. Throughout this series one-half cubic centimeter of this suspension was used.

RESULTS

Series I (Fig. $1A_1, B_1, C_1$).—A bronchogram was obtained five minutes after intratracheal injection. The trachea and the larger bronchi are well visualized, including their finer branches. Immediately after the production of the embolus, the second exposure was made. The opaque material has been squeezed into the terminal radicals. The upper, middle, and lower main bronchi are invisible. The third film was taken eight minutes later showing little change, except more bullous dilatations of the finer bronchi and patches of emphysema as a result of incomplete bronchial obstruction without infarction.[3] In another experiment, in which only the upper branches were visualized, the same scattering of the iodochloral was observed, immediately, three minutes, and ten minutes after the embolism (Fig. $1A_2, B_2, C_2$). In a third set the

Presented before the Central Society of Clinical Research, Chicago, Ill., Nov. 8, 1941.

typical pattern of the bronchial tree is shown again, before, three minutes, and ten minutes after embolism (Fig. 1A_3, B_3, C_3). Twelve experiments showed an identical pattern. They were accompanied by the classical dyspnea and cyanosis of pulmonary embolism.

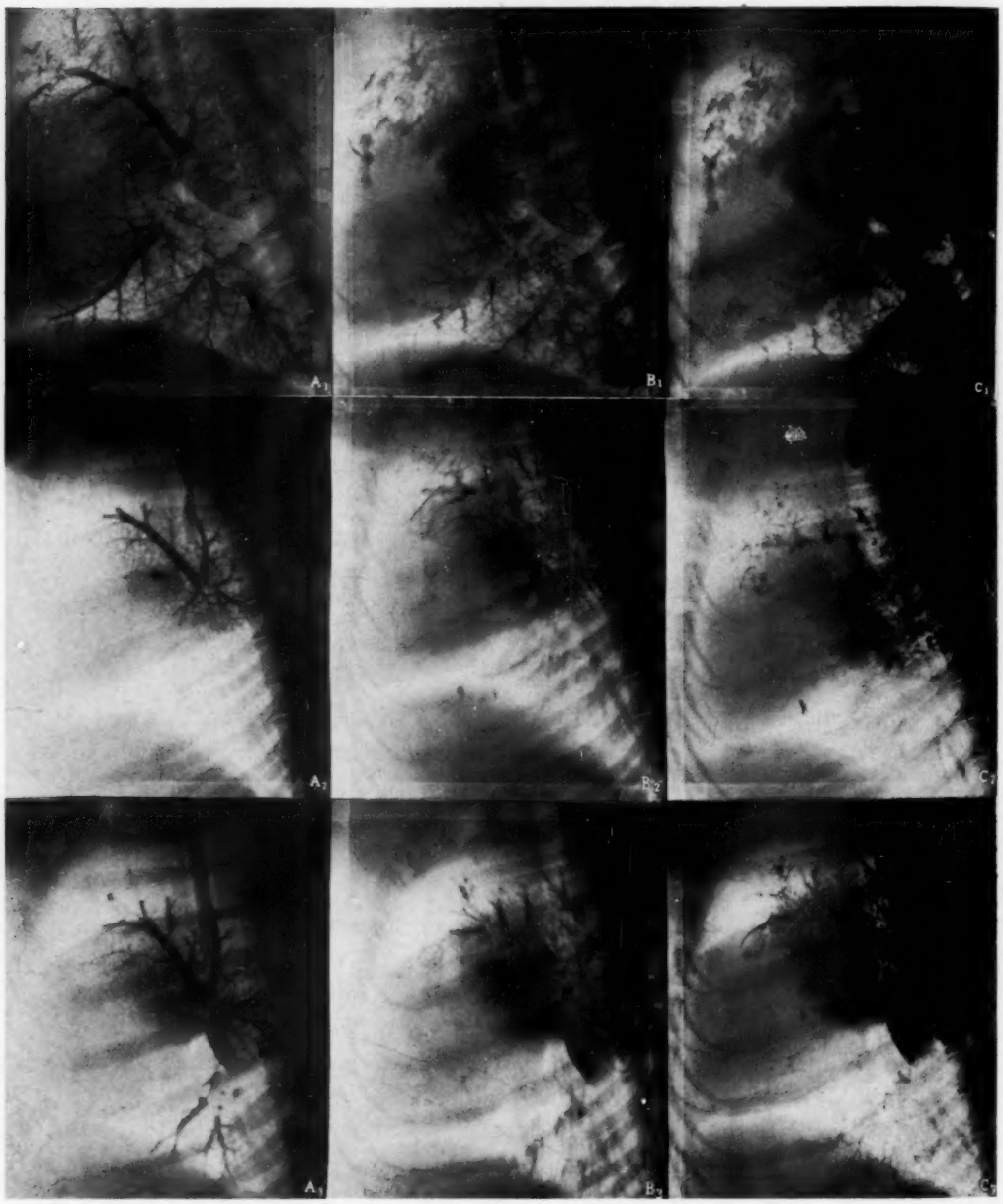

Fig. 1.—These films report three separate experiments. A_1, The bronchograms were obtained five minutes after an intratracheal injection of 5 cm. of iodochloral. The trachea and the larger bronchi are well visualized. In A_2 the lower bronchi did not fill; in B the films were obtained immediately after the production of the embolus. The opaque material has been squeezed out of the larger bronchi into the terminal radicals. The upper, middle, and lower main bronchi are invisible. C, The third series of films were taken eight or ten minutes after the production of the embolus; the pattern has remained the same. Patches of emphysema are visible in these three films, which may well be the result of incomplete bronchial obstruction.

Series II (Fig. 2).—After the visualization of the bronchi, the trachea of the animal was clamped with a six-inch, curved forceps causing marked dyspnea and cyanosis. Films were obtained at the height of respiratory distress, immediately after, and five minutes after release of the clamp.

Three such experiments were performed; none of them showed any change in the pattern of the bronchial tree. Cyanosis and dyspnea cannot be responsible for the bronchial spasm seen in the previous series.

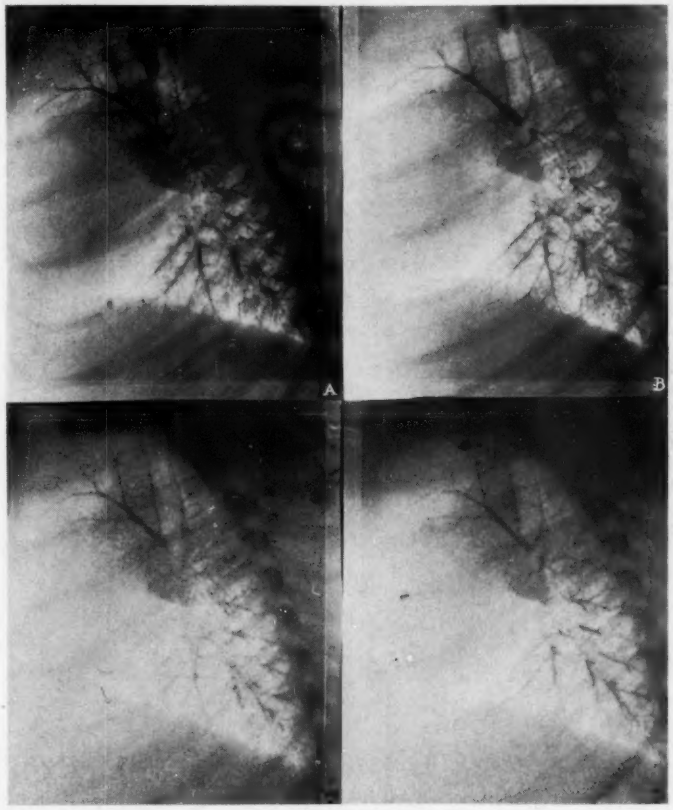

Fig. 2.—*A*, Control film; *B*, film was obtained at the height of respiratory distress after the trachea of the dog was clamped with a six-inch curved forceps, which caused marked dyspnea and cyanosis; *C*, immediately after the release of the clamp; *D*, five minutes after the release of the clamp.

Series III (Fig. 3).—After a control film, showing a good visualization of the upper bronchus, a bilateral vagal section was done in the neck and the second film obtained two minutes later. There seemed to be a slight dilatation of the main upper bronchus. The third film was obtained three minutes after the production of an embolus, showing no change in the caliber of the main bronchus. The last film was taken five minutes after the embolus, indicating no change in the bronchial tree.

Bilateral vagal section, performed in four experiments, prevented the appearance of a pattern seen in the first series and interpreted as bronchospasm.

Series IV (Fig. 4).—After a control film showing visualization, $\frac{1}{75}$ gr. of atropine was injected intravenously and a film obtained five minutes later. There was no change in the pattern. Then the emolus was produced. The third film was taken immediately after the injection, showing slight scattering in the lower lobe. Two and five minutes later the pattern is still well maintained, although the dog died immediately after the last exposure.

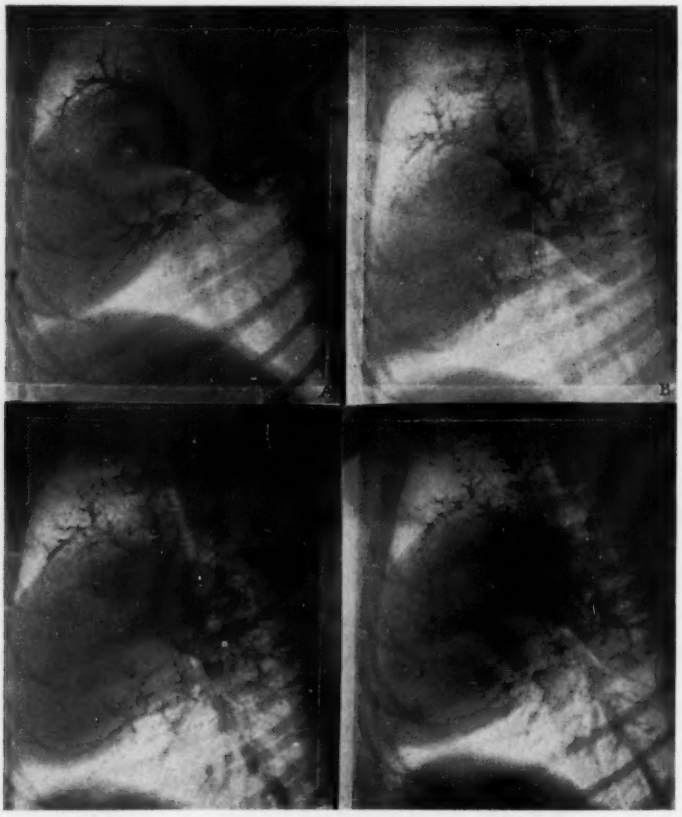

Fig. 3.—*A*, A control film was obtained showing good visualization of the upper bronchus. *B*, Film obtained two minutes after vagal section, the upper main bronchus seems to be more relaxed than in the control film, otherwise the pattern is the same. *C*, Was obtained three minutes after the production of the embolus, showing no change in the caliber or pattern of the main bronchus. *D*, This film was obtained five minutes after the production of the embolus; the original pattern is still being maintained.

In a total of twelve experiments $\frac{1}{75}$ gr. of atropine preserved the bronchial pattern in seven and failed to do so in five instances.

Series V.—In using $\frac{1}{35}$ gr. of atropine in a series of nine dogs, six of them obtained a complete protection from bronchial spasm. In Fig. 5, a control film was obtained, a second one five minutes after the atropin was injected, the third film immediately after the embolus was produced, and the last one three minutes later, at which time the animal died. There is no evidence of bronchial spasm in these films.

As further evidence that these dogs die of pulmonary embolism and yet exhibit no bronchial spasm, we show Fig. 6 in which, after a control

film, and a second one after atropine, 1/75 gr., the embolism is produced. This did not affect the caliber of the bronchus, although some of the material must have trickled out. The fourth film was taken five minutes after the embolus and three seconds after the visualization of the right heart was undertaken by a method reported previously.[2] A comparison with the films shown in our previous report discloses the fact that this is a markedly enlarged right heart, a true cor pulmonale, which coexists with the absence of bronchial spasm prevented by 1/35 gr. of atropine.

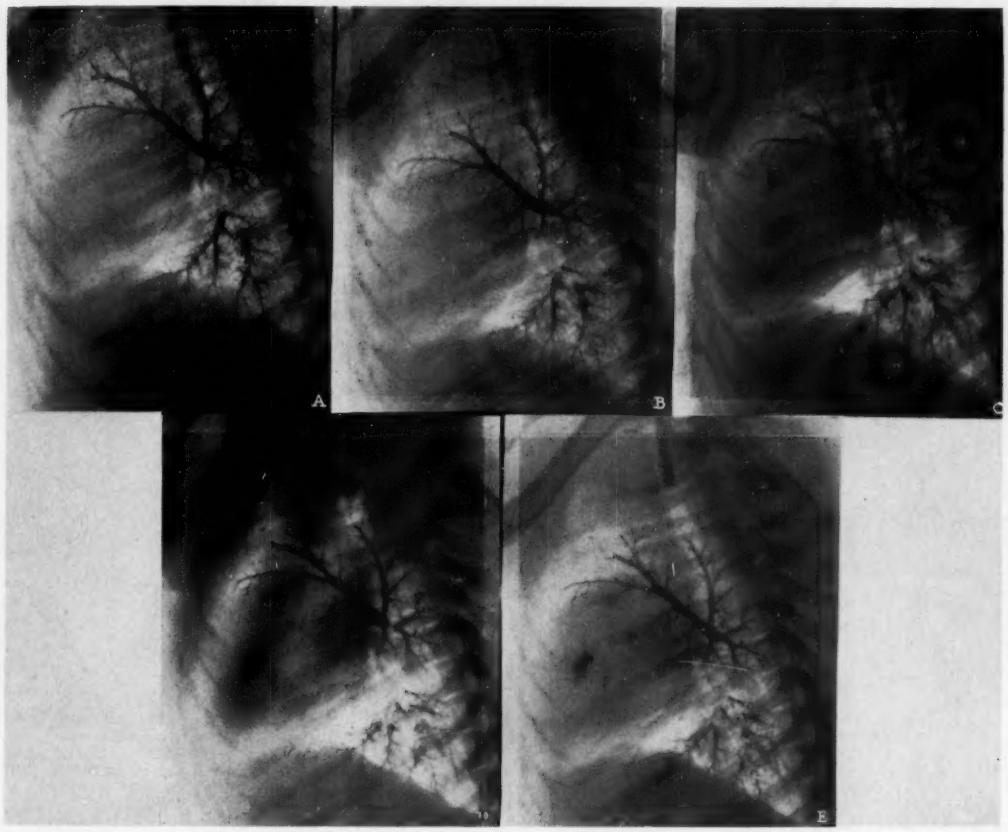

Fig. 4.—*A*, Control film showing very good visualization of the bronchial tree. *B*, Film taken five minutes after intravenous injection of 1/75 gr. of atropine; there is no change in the pattern of the bronchi. *C*, Film obtained immediately after the production of the embolus with a maintained bronchial pattern; there is perhaps a slight scattering of the material in the lower lobe. *D*, Film obtained two minutes after the embolus, showing no bronchial spasm. *E*, Film obtained five minutes after the production of the embolus; the pattern is fully maintained although the dog died immediately after this exposure.

Series VI.—In a series of seven dogs, papaverine, 1/2 gr., was given intravenously to test its protective action against bronchial spasm. Of the seven dogs, four obtained a result from this medication but the protection was never as complete as with atropine. In Fig. 7 a good bronchial pattern was obtained which was followed by a second film five minutes after the intravenous injection of 1/2 gr. of papaverine. Immediately after the embolus the third film was obtained, which showed definite scat-

tering although the pattern of the major bronchi was not lost as in the films obtained in the first series without medication. A film taken five minutes later shows a definitely improved pattern as if the papaverine had had a delayed action. The action is slower and, as will be discussed, of a different nature than that of atropine.

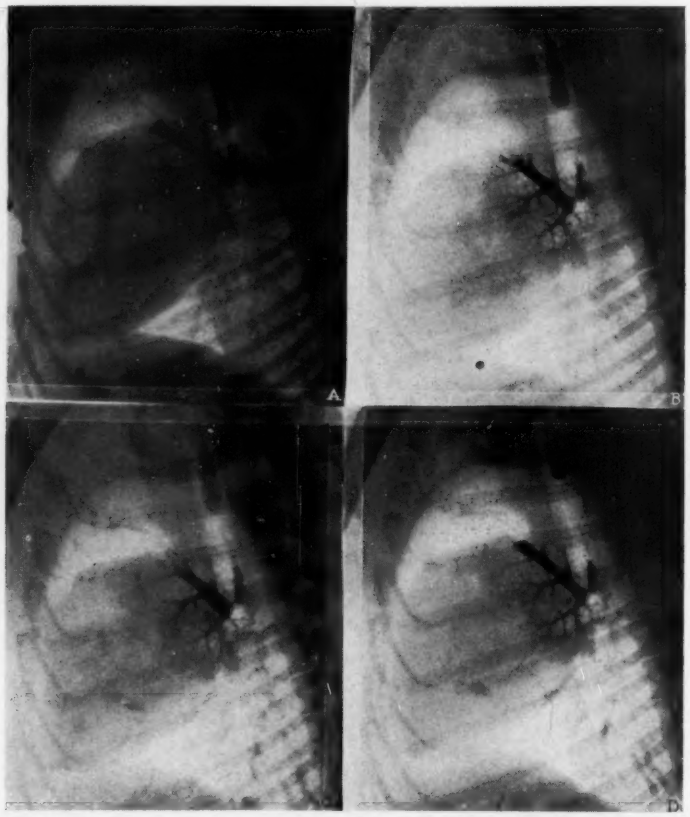

Fig. 5.—*A*, The upper main bronchus is well visualized. *B*, Film obtained five minutes after the intravenous injection of 1/65 gr. of atropine. *C*, This film was obtained immediately after the production of the embolus. *D*, Exposure made three minutes after the production of the embolus, at which time the animal died; there is no evidence of bronchial spasm in these films.

Series VII.—In a series of nine dogs in which the prevention of bronchial spasm was attempted with a medication of atropine, 1/75 gr., and papaverine, 1/2 gr., only six obtained good protection. This has been shown in Fig. 8. The four films were taken before, five minutes after the drugs, immediately after the production of the embolus, and four minutes later in an agonal condition. The prevention of bronchial spasm was satisfactory. In Fig. 9, after a control film, the drugs were injected; the second film was taken immediately after the embolus, the third one five minutes later. There is no protection from spasm in these films.

SUMMARY OF EXPERIMENTS

In a total of sixty-three dogs, 316 exposures were made; some of these had to be discarded for technical reasons, so that fifty-three dogs were

available for study. A clear-cut bronchial spasm was demonstrated after embolism in every instance; the bronchial pattern was distorted and the opaque substance scattered in all of them. Using this series of twelve dogs, in which bronchial spasm was obtained in 100 per cent as a control, the protecting or modifying methods gave the results shown in Table I.

While the series is small, the obtained percentages approximate closely the larger series obtained previously,[1] in which the death of the animal was prevented from embolism by employing vagal section, atropine, or papaverine. Possibly a higher dose of atropine, $\frac{1}{6}$ gr., might have resulted in a higher incidence of protection from spasm.

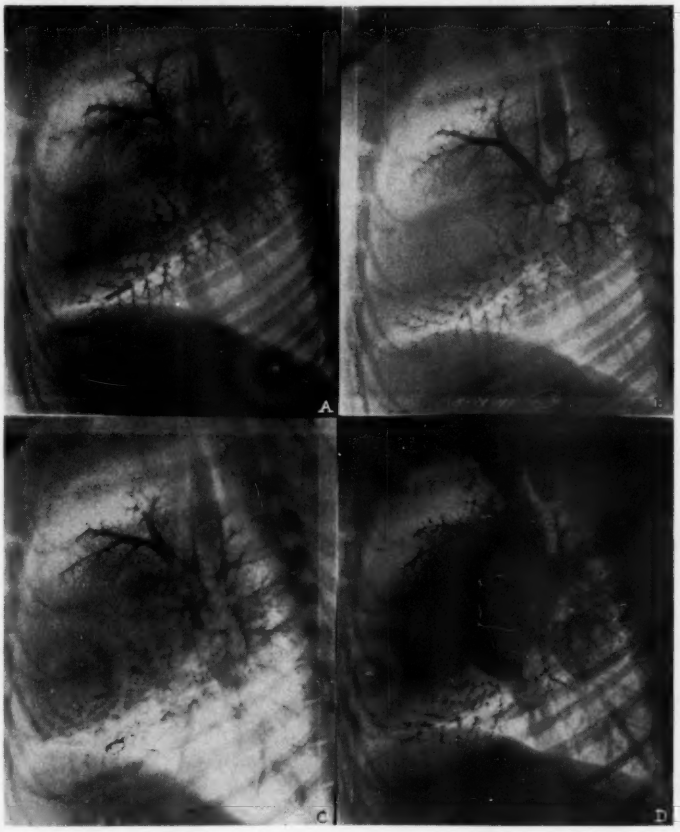

Fig. 6.—*A*, Control film. *B*, Film obtained after the intravenous injection of atropine, $\frac{1}{75}$ gr. *C*, Immediately after the production of the embolus which did not affect the caliber of the bronchus, although some of the opaque material must have trickled out. *D*, Film obtained five minutes after the production of the embolus and three seconds after the visualization of the right heart; this last film shows that a true cor pulmonale has been produced and yet bronchial spasm has been prevented by $\frac{1}{75}$ gr. of atropine.

COMMENT

The production of pulmonary embolism followed by visualization of the bronchial tree reveals in each instance a disappearance of the visible pattern of the main bronchi. That this is due to bronchial spasm is shown by the experiments in which this change in pattern was inhibited,

TABLE I

SUMMARY OF EXPERIMENTS

NUMBER OF DOGS	METHOD OF PREVENTION	PROTECTION FROM SPASM IN PER CENT
12	--------	0
12	Atropin, gr. 1/75	58
9	Atropin, gr. 1/35	66
7	Papaverine, gr. ½	40
9	Atropin, gr. 1/75 plus papaverine, gr. ½	66
4	Bilateral vagal section	100
53		

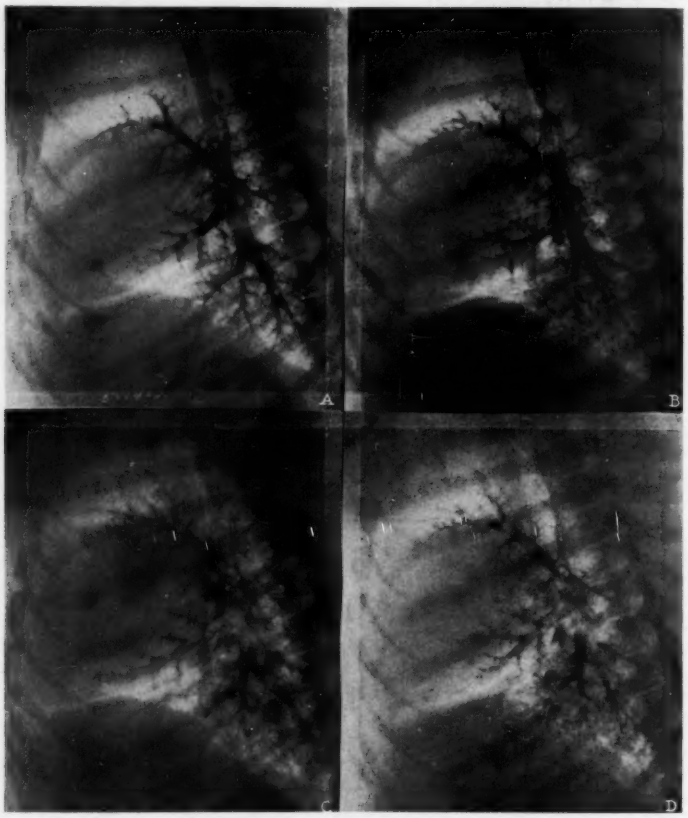

Fig. 7.—*A*, Control film showing a good bronchial pattern. *B*, Film obtained five minutes after the intravenous injection of ½ gr. of papaverine; there is no obvious change in the pattern. *C*, Film obtained immediately after the production of the embolus; this film shows definite scattering, particularly in the lower lobe, although the pattern of the major bronchi has not been lost. *D*, Film taken five minutes after the production of the embolus showing a definitely improved pattern, as if the papaverine had begun to act; this series of films would indicate that the action of papaverine is more delayed than that of atropine.

either by bilateral vagal section or by 1/35 gr. of atropine. The spasm is not due to hypernea or anoxemia, as mechanical obstruction to the trachea fails to produce the marked scattering of the opaque substance into the final radicals.

As vagal stimulation produces bronchial constriction and surgical or pharmacologic block of the vagus abolishes the bronchial spasm, we

have here another instance of reflex vagal impulses occurring during pulmonary embolism. We have discussed in a previous paper the possible sources of such reflexes.[1] They may originate from the hypertension in the pulmonary artery,[4] from the powerful myelinated receptors of the bronchial musculature,[5] from the congestion of the lung,[6] and from pleural irritation.[7] These reflexes have effects on the heart, on the pulmonary vascular bed, and on the bronchi, as shown in this report.

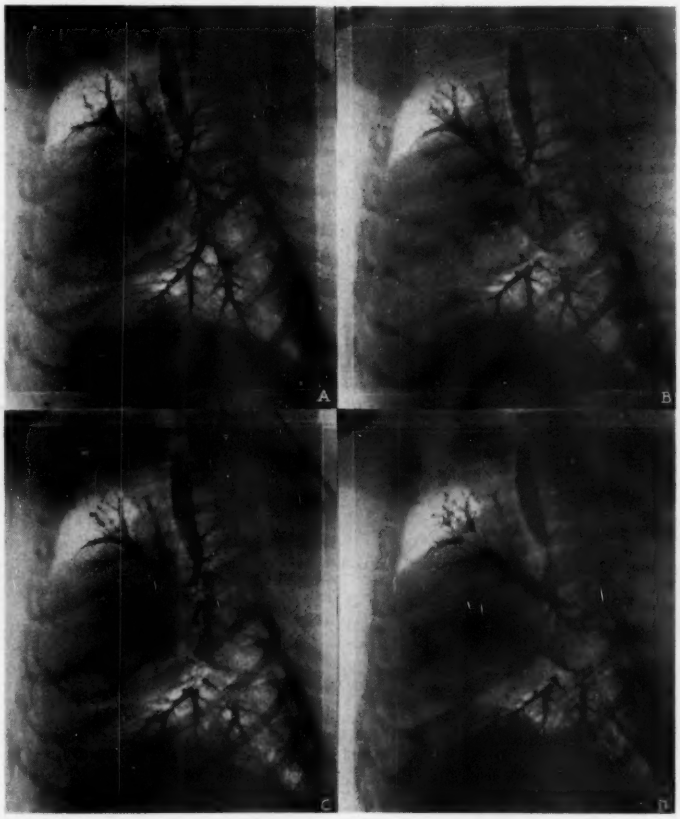

Fig. 8.—*A*, Control film. *B*, Film obtained five minutes after intravenous injection of atropine, 1/75 gr., and papaverine, ½ gr. *C*, Film obtained immediately after the production of the embolus showing some scattering but still a maintenance of the pattern. *D*, Film obtained four minutes after the production of the embolus with a well-maintained pattern; the pattern has improved in this last film.

Hardly any attention has been given to this bronchial factor in the past. Singh[8] reported the presence of bronchial spasm during air-embolism and recommended epinephrine for its relief. Neither atropin nor vagal section abolished the spasm in his experiments. Epinephrine in our previous experiments[1, 2] exerted a deleterious effect on the animal subjected to pulmonary embolism. It is true that it stimulates the sympathetic bronchodilators and relaxes the bronchial tree, but it also raises the pressure in the pulmonary artery and precipitates pulmonary edema. Its clinical use in pulmonary embolism is inadvisable.

Binet and Burstein[9] studied bronchial spasm as a result of anaphylactic shock, histamine and acetyl choline injections, and pulmonary embolism. They used an intratracheal cannula during their experiments and obtained kymographic records, which are greatly influenced by respiratory movements. We repeated these experiments but felt that our present method of bronchography yielded a more definite and simple graphic record.

That papaverine relaxes bronchial musculature has been known ever since Pal's initial observations on this drug.[10] In our experiments its actions were slower and much less marked than that of atropin. Nevertheless, its use is highly important because of its effect on coronary flow and the pulmonary vascular bed.[2] According to Linder and Katz[11] the drug inhibits ventricular fibrillation, which is frequently the immediate cause of death from pulmonary embolism.

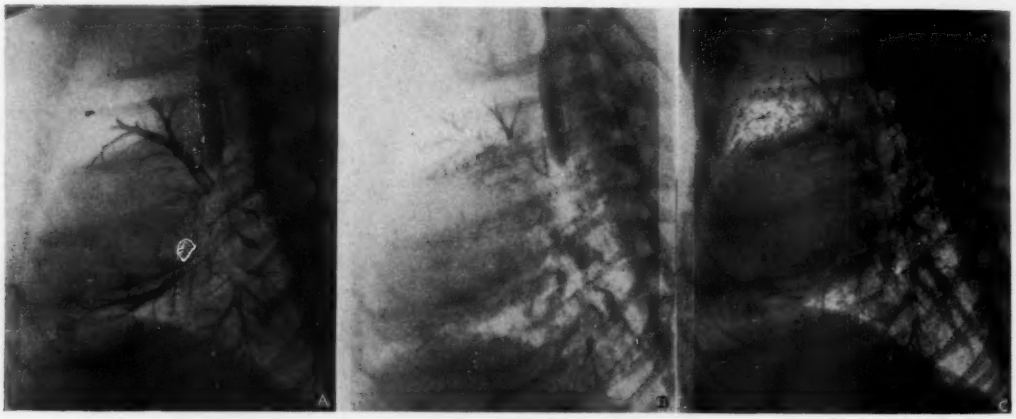

Fig. 9.—*A*, Control film. *B*, Five minutes after the intravenous injection of 1/75 gr. of atropine and ½ gr. of papaverine; the embolus was produced immediately before this film was taken and shows a marked scattering of the material and, thus, no protection from spasm. *C*, Film obtained five minutes after the production of the embolus in which there is still a great deal of scattering, although some recovery of the original form of the bronchial tree. This group of films shows that the medication used has not been effective in preventing bronchial spasm.

CLINICAL APPLICATIONS

We have repeatedly stressed our belief that reflexes originating at the time of pulmonary embolism contribute to the causes of death and have suggested simple emergency measures for its control. Outside of oxygen, which is obviously helpful for cyanosis and dyspnea, intravenous injections of atropine (1/60 to 1/75 gr.) and papaverine (½ gr.) were recommended.[12] The appearance of bronchial spasm, concomitant with pulmonary embolism, has been seemingly ignored in the past and can be inhibited, at least in the animal experiment, by atropin.

The bronchial asthma of pulmonary embolism explains the frequent finding of atelectatic areas in the x-ray films of patients suffering from pulmonary embolism. The vagal stimulus produces not only bronchial

constriction but also bronchial secretion. The bloody mucous plug in the bronchi seen at autopsies of patients dead from pulmonary embolism is the cause of atelectasis and patchy bronchopneumonias. Haight and Ransom[13] have recently re-emphasized the prompt recognition and treatment of retained bronchial secretions following operations by posture, coughing, tracheobronchial suction, and bronchoscopy. They stress hypoventilation as the most important factor in the retention of bronchial mucus. Cutler[14] for many years has held the embolic theory of postoperative lung reactions, feeling that small emboli may pass through the lymphatics of the diaphragm and cause pulmonary complications. Our present series of experiments suggest that some of these bronchial obstructions may be of reflex nature, either originating from pulmonary emboli or possibly from intra-abdominal sources of irritation. Thus, it has been sufficiently established that distention of the stomach[15] or increased pressure in the biliary system[16] produces vagal effects on the heart, which can be abolished by atropine. Experiments are contemplated in the future to see whether an effect on the bronchi can be produced by intra-abdominal manipulations.

The use of atropine in the presence of bronchial obstruction and hypersecretion may be objected to by many who feel that this drug increases the viscosity of the bronchial mucus and hinders evacuation. In the first few minutes and hours following pulmonary embolism, however, its administration dilates the bronchi and suppresses secretion. In a total of twenty-eight cases of pulmonary embolism observed at St. Luke's hospital, the atropine-papaverine mixture was administered in every instance. The drugs were given immediately after the recognition of the embolus and four to five days after, three times a day. No massive or patchy atelectasis was seen in this group, indicating that at least this medication does not increase bronchial obstruction to a harmful degree.

SUMMARY

The bronchial tree of the dog was visualized and the effect of pulmonary embolism on the pattern of the bronchial tree was studied. It was found that a powerful bronchoconstriction was produced during embolism, which could be abolished by bilateral vagal section and often by sufficient doses of atropin. Mechanical obstruction to the trachea failed to produce bronchial spasm. Papaverine failed to protect the bronchial tree from this reflex spasm in most instances. These experiments emphasize the existence of widespread autonomic reflexes which occur within the distribution of vagal fibers. The suppression of these reflexes decreases the morbidity and mortality from pulmonary embolism.

Our thanks are due to Miss Lillian Ryan, R.N. of the Neurocirculatory Clinic and Mr. Art Hesse for their valuable technical assistance.

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REGIONAL LYMPHATIC METASTASES OF CARCINOMA OF THE GASTROINTESTINAL TRACT*

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THE purpose of this paper is to compare the gross and microscopic characteristics of carcinoma of the gastrointestinal tract to the incidence of regional lymph node metastases. For a more detailed discussion of the anatomy of the lymphatics of the gastrointestinal tract and the location of the lymphatic metastases incident to carcinoma, the reader is referred to the previous communications upon this subject.[1-3]

This study is based upon the dissection and examination of all the lymph nodes from 152 operative specimens of carcinoma of the gastrointestinal tract, including 53 gastric, 46 colonic, and 53 rectal specimens. The lymph nodes were dissected from each specimen after they had been visualized (Fig. 1) by clearing by the Gilchrist and David[4] modification of the Spalteholtz method. All nodes were examined microscopically and the results charted upon diagrammatic drawings, upon which every node was indicated (Figs. 2, 3, 4, and 5). The presence or absence of regional lymph node metastases was then correlated with (1) the age of the patient, (2) duration of symptoms, (3) gross type of neoplasm, (4) size, (5) circumferential extent (of colonic and rectal cases), (6) depth of infiltration, (7) microscopic type, and (8) the degree of cellular differentiation.

Regional lymph nodes which may be isolated thus go unnoticed by the usual method of dissection. Many large nodes were found to be inflammatory and many small impalpable nodes were found to contain metastatic carcinoma. Unless a lymph node was definitely replaced by carcinoma, it was impossible to determine without microscopic examination whether it was involved. These observations demonstrate clearly that operative procedures should not be minimized because of the absence of palpable lymph nodes.

As a result of this special method of investigation, 75.5 per cent of the gastric carcinomas, 60.87 per cent of the colonic carcinomas, and 64.2 per cent of the rectal carcinomas were found to have regional lymph node metastases. There were 30.2 nodes per specimen isolated in the gastric series in comparison to 52.07 nodes for the colonic series, and 67 nodes per specimen for the rectal group. The greater the number of nodes isolated in the individual groups, the higher the incidence of lymphatic metastases found. The comparative groups are shown in Table I.

*This study was aided in part by a grant from the James and Elizabeth Inglis Fund for Surgery Research.
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The carcinomas of the colon should have the most favorable prognosis of the entire group. They not only had the lowest incidence of regional lymph node metastases in our series, but they also had the largest number of cases in which only one lymph node was involved. Eleven of the colonic neoplasms were found to have only one positive node which was located close to the primary site in the majority of the cases. This was also true in 5 of the gastric cases and 6 of the rectal.

Not only did the gastric and rectal series have a higher incidence of lymphatic metastases, but they also had a higher incidence of microscopic infiltration into blood vessels in the absence of gross hematogenous metastases. There was an incidence of 15 per cent microscopic infiltration of blood vessels in both the gastric and rectal series, and only 10 per cent in the group of colonic carcinomas.

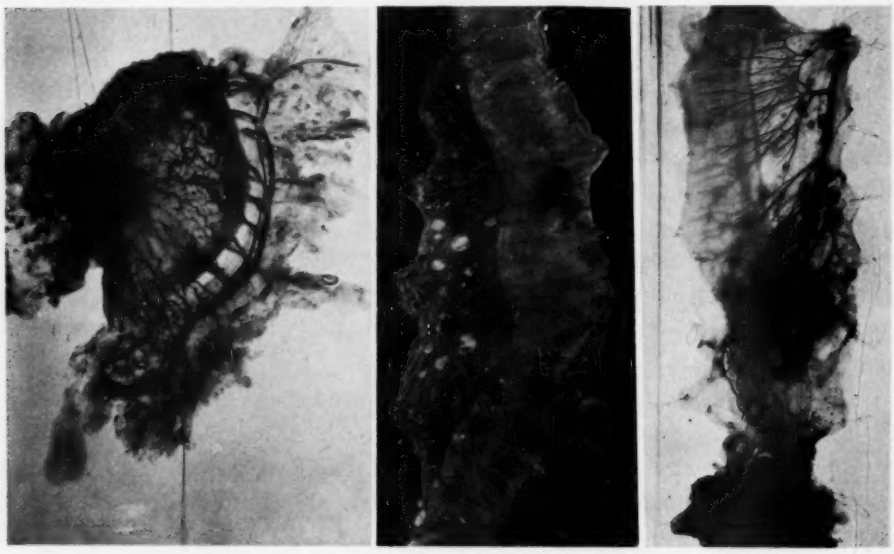

Fig. 1.—Photographs of the cleared operative specimens of the stomach, sigmoid colon, and rectum, demonstrating the visualization of the lymph nodes following clarification.

AGE AND METASTASES

The view that neoplasms tend to be more malignant in the younger age groups was substantiated by this study. In dividing the cases into two groups, those above and those below 50 years of age, the patients in the latter group had the higher incidence of metastases. Seventy-seven per cent of the gastric carcinomas in patients below 50 years of age had metastasized, in comparison to 75 per cent of those above; 75 per cent of the colonic cases in the younger age group had metastasized, in comparison to 55.8 per cent in the older age group, and 70 per cent of the rectal carcinomas in the first group had metastasized in comparison to 60.6 per cent in the second.

TABLE I

LOCATION	NUMBER OF CASES	AVERAGE NO. OF NODES PER SPECIMEN	AV. NO. NODES PER SPECIMEN IN GROUP WITH METASTASES	AV. NO. NODES PER SPECIMEN IN GROUP WITHOUT METASTASES	INCIDENCE OF REGIONAL LYMPH NODE METASTASES
Stomach	53	30.20	32.8	22.4	75.50
Colon	46	52.07	59.4	41.4	60.87
Rectum	53	67.00	66.2	67.5	64.20

DURATION OF SYMPTOMS

There was no relation between the duration of symptoms and the presence of lymph node metastases. It was noted that duration of symptoms diminished progressively from the stomach downward. The period between the onset of symptoms and the time of seeking medical

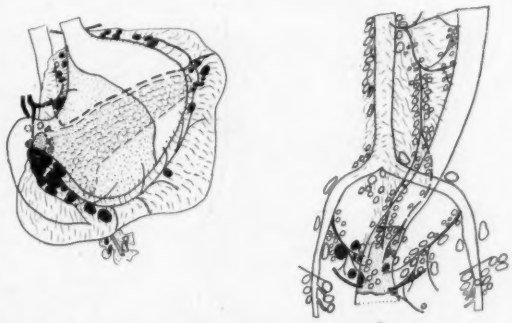

Fig. 2.—*A*, Line drawing demonstrating the zonal distribution of the lymphatic metastases in the necropsy specimen of a carcinoma of the stomach; *B*, line drawing of a necropsy specimen of a carcinoma of the anal canal, demonstrating the lateral zone of metastases.

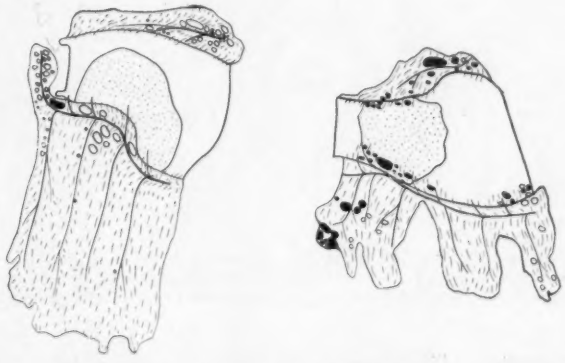

Fig. 3.—Line drawings of operative specimens of carcinoma of the stomach demonstrating variations in the incidence and zonal distribution of the lymphatic metastases.

aid was longest in the stomach group. The average duration of symptoms was 13+ months in the gastric group, 10+ months for the colonic group, and 8+ months for the rectal group. The patients with the shortest duration of symptoms do not always have the most favorable prognosis. Many of these carcinomas are fast growing and produce symp-

toms early. Many patients with symptoms present over a long period often have a more favorable prognosis. These are cases in which the neoplasm is slow-growing, is of a low degree of malignancy, and metastasizes late. Review of the histories of the 53 patients with carcinoma of the stomach revealed 5 with symptoms over a year's duration, who were free from lymphatic metastases. Several of these had had symptoms for two and three years, while 6 patients with symptoms ranging from one to three months had regional lymph node involvement. There was an incidence of lymphatic metastases in the colonic group of only 40 per cent (4 of 10 cases) in patients who had had symptoms for

Fig. 4.—Line drawings of representative cases of operative specimens of carcinomas located in the various regions of the large intestine demonstrating the incidence and routes of their lymphatic metastases. (Courtesy of *Annals of Surgery.*)

two years or more, in contrast to an incidence of 73 per cent metastases (8 of 11 cases) in patients with symptoms of three months or less. Similarly, in the rectal series there were 3 patients with symptoms of one month or less who had had lymph node metastases. There were several other patients without any symptoms who were found to have rectal carcinomas which were later discovered to have metastasized. There were 4 patients with symptoms of one year's duration, one of one and one-half year, and another of two years, all of whom were free

from lymph node metastases. One of these patients had been given up as hopeless one and one-half years prior to admission to this hospital. These observations show that operative procedures should not be minimized because of short duration of symptoms and that patients with symptoms over a long period of time should not be denied operation because of this fact alone.

GROSS TYPE AND METASTASES

Carcinomas of the gastrointestinal tract were classified according to their gross characteristics into three groups: (1) Neoplasms characterized primarily by the presence of ulceration; (2) the polypoid, fungating neoplasms which tend to grow intralumenly; and (3) the sessile, plaquelike neoplasms which are invasive in character. In the stomach series, there were 6 neoplasms of the ulcer type, of which 2 were found microscopically to have arisen upon peptic ulcers, and a third

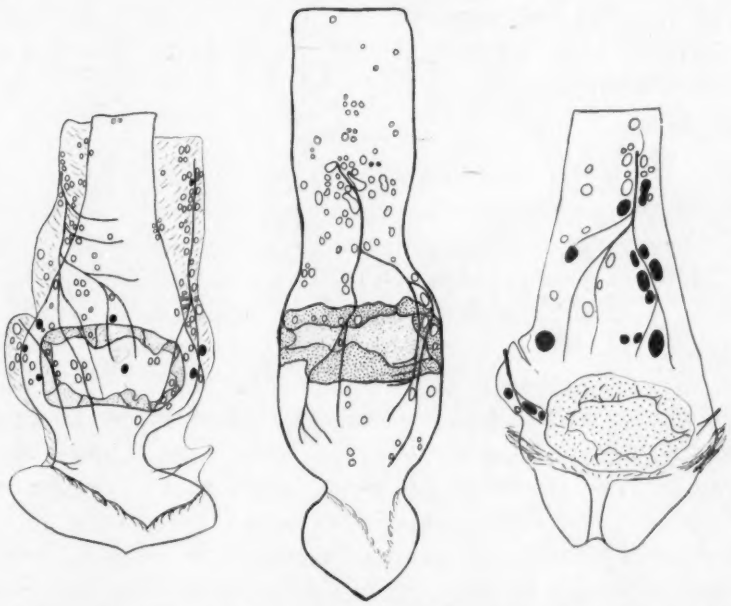

Fig. 5.—Line drawings of representative cases of operative specimens of carcinomas of the rectum demonstrating several of the variations noted in their lymphatic metastases.

in association with two nearby peptic ulcers. There were no cases in the colonic series within this group, and only three rectal neoplasms of the ulcer type. These were all large excavating ulcers. The polypoid neoplasms formed the largest group. There were 25 polypoid neoplasms of the stomach, 40 of the colon, and 28 of the rectum. The sessile neoplasms formed the intermediate group in regard to incidence. There were 22 sessile neoplasms of the stomach, 6 of the colon, and 21 of the rectum.

The 9 ulcer cases form too small a group from which to draw conclusions, but it is of interest to know that 66.6 per cent of the ulcer type in the stomach, and 33.3 per cent of those in the rectum had regional lymph node metastases.

In the polypoid group there was an incidence of metastases of 60 per cent in the stomach, 57.5 per cent in the colon, and 53.5 per cent in the rectum, while in the sessile group there was an incidence of metastases of 95.4 per cent in the stomach, 83.3 per cent in the colon, and 80.9 per cent in the rectum. It is of further interest to note that the incidence of sessile neoplasms in the gastric group (Table II) is much higher than it is in the other two groups, and that the incidence of polypoid neoplasms in the colonic group is the highest. As might be expected, the incidence of metastases is greatest in the gastric group and least in the colonic. Because of the above facts, it is mandatory that operative resections include all of the regional gland-bearing areas in cases of sessile neoplasms. Even though the incidence of metastases is less with the polypoid neoplasms, there is no method of determining which have or have not metastasized, consequently, they too must be observed with suspicion.

TABLE II

INCIDENCE OF METASTASES

	STOMACH	COLON	RECTUM
Ulcer	6 (66.6 per cent)	0 (0.0 per cent)	3 (33.3 per cent)
Polypoid	25 (60.0 per cent)	40 (57.5 per cent)	28 (53.5 per cent)
Sessile	22 (95.4 per cent)	6 (83.3 per cent)	21 (80.9 per cent)

SIZE AND METASTASES

There was no relation between the size of the neoplasm and the presence of metastases. It is of interest to note that the small neoplasms were just as likely to metastasize as the larger ones. In order to arrive at a more accurate figure concerning their relative sizes, their areas were computed rather than using references to any one diameter. The carcinomas of the cecum were the largest neoplasms of the entire gastrointestinal tract, averaging 46.56 sq. cm. The next largest were found in the stomach, which averaged 42.45 sq. cm. The neoplasms of the right colon were larger than those of the left. The average size of neoplasms with metastases in the right colon was 32.75 sq. cm. in comparison to 39.5 sq. cm. in those without, while the average of the neoplasms of the left colon with metastases was 22.11 sq. cm. compared to 31.73 sq. cm. in those without. This demonstrates that the incidence of metastases may be just as great, or greater, in the small neoplasm as in the large. The comparison, of course, eliminates automatically the large inoperable carcinomas. The smallest carcinomas were those in the rectum, which averaged 26.2 sq. cm. Differences in the size of the neoplasms above are not

the result of any inherent factor within the neoplasm, but rather the result of the location in which the neoplasm is found. The neoplasms of the cecum were the largest, because the caliber of the cecum is the largest, and neoplasms may exist there a long time before producing symptoms.

Analysis of the sizes of individual neoplasms shows those occurring in the fundus of the stomach to be considerably larger than any of the others, but when the areas of these were averaged with the smaller neoplasms occurring at the pylorus, the average for the entire gastric group was then second in size to those of the cecum. It is to be expected that neoplasms of the rectum are the smallest because of their clinical behavior and their accessibility to medical examination.

Further analysis of the data further revealed that in the gastric group 84.7 per cent of the neoplasms larger than average size had metastasized, compared to 66.6 per cent of those smaller than average size. Furthermore, 5 of the 6 largest neoplasms, and 4 of the 6 smallest neoplasms were found to have metastasized. In the rectal group, the 10 smallest and the 10 largest carcinomas were compared, and in each group there were 6 cases with and 4 cases without metastases. Thus, the size of the neoplasm is no indication of metastases.

CIRCUMFERENCE INVOLVED AND METASTASES

It is of interest to note the comparison in the amount of circumferential spread of the neoplasm in the rectum and the colon. Since the lymph channels follow the course of the intramural radial blood vessels around the circumference of the bowel, carcinomas of the rectum and colon tend to be annular. The carcinomas of the rectum were divided into four groups, depending upon the percentage of bowel circumference infiltrated. As will be seen from Table III, there was an increasing tendency to metastasize as more bowel circumference was involved.

TABLE III

PERCENTAGE OF CIRCUMFERENCE INVOLVED	NUMBER OF CASES	WITH METASTASES	PERCENTAGE METASTASES
0- 25 per cent	4	2	50.0
25- 50 per cent	10	6	60.0
50- 75 per cent	22	14	63.6
75-100 per cent	17	12	70.6

Many of the rectal neoplasms had only infiltrated from one-fourth to one-half of the bowel circumference, and 4 of them had involved less than one-fourth of the circumference.

In contrast, there were none of the colonic group with less than 25 per cent of the circumference involved and the majority of the neoplasms (37 out of 46) were completely annular. In only 3 instances was less than 50 per cent of the lumen involved, and 3 were included in the group

of 75 to 100 per cent circumferential involvement. Because of the large number of completely annular carcinomas in the colon, the relation between circumferential involvement and metastases is not striking. However, of the 3 cases with 25 to 50 per cent involvement of the circumference, only 1 had metastasized.

DEPTH OF INFILTRATION AND METASTASES

Gabriel, Dukes, and Bussey[5] classified carcinomas of the rectum into Groups A, B, and C. Group A included carcinomas infiltrating well into the wall but not into the perirectal tissues; Group B, those extending into the perirectal tissue; and Group C, those having positive lymph node metastases. The patients in 91 per cent of Group A cases and 64 per cent of Group B cases were alive five years or more following operative removal, whereas only 18 per cent survived five years in Group C. There were 30 cases in our series in which the malignancy was confined to the rectal wall and of these, 13 (43.3 per cent) had metastasized to the regional lymph nodes; whereas, there were 22 cases with infiltration into the perirectal tissues, of which 20 (90.9 per cent) had metastasized.

The contrast between the malignant character of the carcinomas of the rectum and those in the colon and stomach is striking. It was shown above that neoplasms of the colon had involved the entire circumference of the bowel in the majority of cases, compared to partial circumferential infiltration in the rectal group. It is noted here that the majority of the rectal neoplasms (30 of 53 cases) had not infiltrated through the bowel wall, while 47 of the 53 gastric cases, and 43 of the 46 colonic cases had infiltrated completely through their respective walls and involved the serosa. This is an ever-present source of free peritoneal metastases and may well be responsible for the better prognosis in carcinoma of the rectum. In 2 of the 5 gastric neoplasms, and 2 of the 3 colonic neoplasms in which the carcinomatous infiltration was confined to the muscular layer only, metastases were also found.

DEGREE OF CELLULAR DIFFERENTIATION (GRADING) AND METASTASES

Our studies (Table IV) substantiated the dictum that the more anaplastic the neoplasm, the higher the incidence of lymphatic metastases.

TABLE IV

GRADE	NUMBER OF CASES	NUMBER OF CASES	PERCENTAGE
1	1	0	0.0
2	70	47	67.1
3	58	43	74.1
4	12	11	91.8

The increasing incidence of metastases proceeding from the colon and rectum to the stomach is shown in Table IV. There was also an increasing incidence of neoplasms of the higher grading in the same order of

TABLE V

LOCATION	INCIDENCE OF GRADE I CARCINOMAS	INCIDENCE OF GRADE II CARCINOMAS	INCIDENCE OF GRADE III CARCINOMAS	INCIDENCE OF GRADE IV CARCINOMAS	INCIDENCE OF OF METASTASES
Colon	0	78.2	19.5	2.1	60.87
Rectum	0	62.2	33.9	1.8	64.2
Stomach	1.8	20.7	58.5	18.8	75.5

colon, rectum, and stomach (Table V). The majority of colonic neoplasms were grade II, or 78.2 per cent, compared to 19.5 per cent grade III carcinomas. The incidence of lymphatic metastases in the colon was 60.87 per cent. In the rectal series the incidence of grade II carcinomas had decreased to 62.2 per cent and grade III carcinomas had increased to 33.9 per cent. The incidence of metastases had also increased to 64.2 per cent. The carcinomas were even more undifferentiated in the gastric group, the majority being grade III. The incidence of grade II carcinomas had decreased to 20.7 per cent, the grade III carcinomas had increased to an incidence of 58.5 per cent, and for the first time there was an appreciable number of grade IV carcinomas, an incidence of 18.8 per cent. The incidence of metastases in the gastric group had also increased to 75.5 per cent.

MICROSCOPIC TYPE AND METASTASES

The majority of the neoplasms were proved histologically to be simple adenocarcinomas. This type composed 16 of the 53 gastric cases, 29 of the 46 colonic cases, and 31 of the 53 rectal cases. The medullary adenocarcinomas had the highest incidence of metastases, 100 per cent in the gastric group and 80 per cent in the colonic group. There were no medullary adenocarcinomas in this particular series of rectal neoplasms. In the gastric group, the scirrhous adenocarcinomas also had an incidence of metastases of 100 per cent. The carcinomas diagnosed adenocarcinoma mucosum also had a high incidence of metastases, 85.7 per cent in the gastric series, 100 per cent in the rectal series, and 75 per cent in the colonic series. The two groups having the lowest incidence of metastases were the adenocarcinomas (simplex) and the papilliferous adenocarcinomas. The adenocarcinomas (simplex) had an incidence of metastases of 56.25 per cent in the gastric group, 62.07 per cent in the colonic group, and 61.2 per cent in the rectal group, while the papilliferous adenocarcinomas had an incidence of metastases of 42.85 per cent in the gastric series, 37.5 per cent in the colonic, and 61.5 per cent in the rectal series.

SUMMARY

An analysis is presented of the incidence of lymphatic spread of 152 carcinomas of the gastrointestinal tract obtained by the dissection of cleared specimens.

An average of 30.2 nodes per specimen was isolated in the gastric, 52 in the colonic, and 67 in the rectal series. A considerably larger number of lymph nodes per specimen was obtained in this way than is possible by the usual method of manual dissection.

An incidence of lymphatic metastases of 75.5 per cent was found in the gastric group, 60 per cent for the colonic, and 64.2 for the rectal.

The view that neoplasms in the younger age groups tend to have a higher incidence of metastases was substantiated by this study.

There was no relation between the duration of symptoms and the presence of lymph node metastases. A comparison of the incidence of lymphatic metastases in carcinoma of the gastrointestinal tract classified according to their gross characteristics, showed that the sessile neoplasms had a much greater tendency to metastasize than the polypoid neoplasms. In the polypoid group there was an incidence of metastases of 60 per cent in the stomach, 57.5 per cent in the colon, and 80.9 per cent in the rectum, while in the sessile group, there was an incidence of metastases of 95.4 per cent in the stomach, 83.3 per cent in the colon, and 80.9 per cent in the rectum.

There was no relation between the size of the neoplasm and the presence of metastases; the smaller neoplasms had just as high an incidence of metastases as the larger ones.

Our studies substantiated the dictum that the more anaplastic the neoplasm, the higher the incidence of lymphatic metastases.

The medullary adenocarcinomas and the adenocarcinoma mucosum had the highest incidence of metastases, while the adenocarcinomas (simplex) and the papilliferous adenocarcinomas had the lowest incidence of metastases.

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A DOUBLE TUBE METHOD FOR DRAINAGE AND FEEDING FOLLOWING GASTRIC RESECTION OR GASTROENTEROSTOMY

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DURING recent years a number of tubes have been devised and advocated for use in the postoperative care of patients undergoing gastric resection or gastroenterostomy. The simplest of these methods is the introduction of a Levin tube into the stomach to which suction is applied usually by means of a Wangensteen suction-drainage system. The advantage of this method is its simplicity and the prevention of gastric distension. However, it will not prevent distension of the very important afferent intestinal loop, neither is it effective for decompression of efferent small intestine, unless it is passed through the anastomotic stoma. This system has the further disadvantage of not permitting early nutritious feeding by means of a jejunal tube.

To offset the disadvantages of this method Abbott and Rawson[1] introduced their double lumen tube, the distal 30 cm. of which is a single lumen tube. This tube is passed into the stomach prior to operation and on completion of the anastomosis the terminal 30 cm. is manipulated into the efferent small intestine (Fig. 1). This tube permits constant gastric suction and early jejunal feeding. Efferent intestinal drainage may be obtained through the lumen used for jejunal feeding. The disadvantage of this tube is that there is no provision for suction drainage from the afferent intestinal loop.

Wangensteen[2] advocates a single lumen tube with forked ends (Fig. 2). This tube permits simultaneous drainage of both afferent and efferent intestinal loops. It makes no provision for early feeding of the debilitated patient by jejunal tube. Fluids introduced through this tube would be equally distributed to afferent and efferent loops.

Based upon the Abbott-Rawson and Wangensteen tubes we have formulated a method at the Metropolitan Hospital, which we believe combines the advantages of each without possessing the disadvantages of either. Use is made of two simple Levin tubes, size 12 F (Fig. 3). These are securely fastened together by means of fine black silk at a point 45 cm. from the tip of tube A and 30 cm. from tip of tube B. At a second point 15 cm. proximal they are again whipped together with black silk. Additional perforations, usually about twelve in number, are added to tube B equally placed from the tip proximally for 45 cm.

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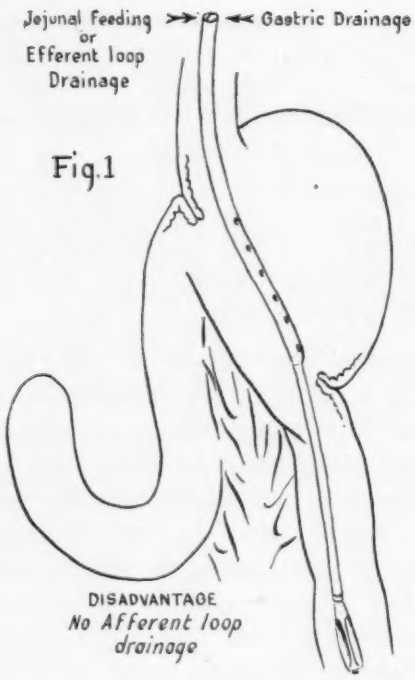

Fig. 1

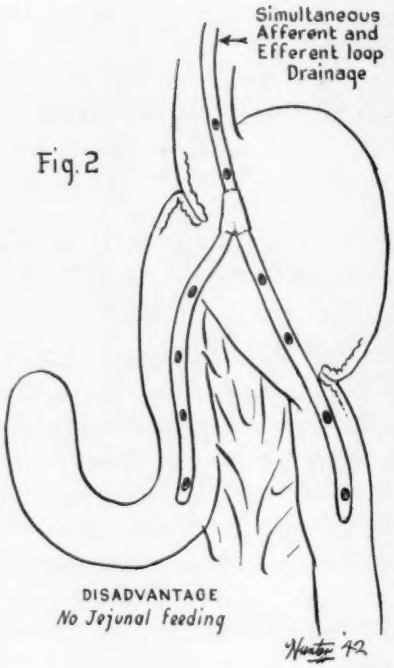

Fig. 2

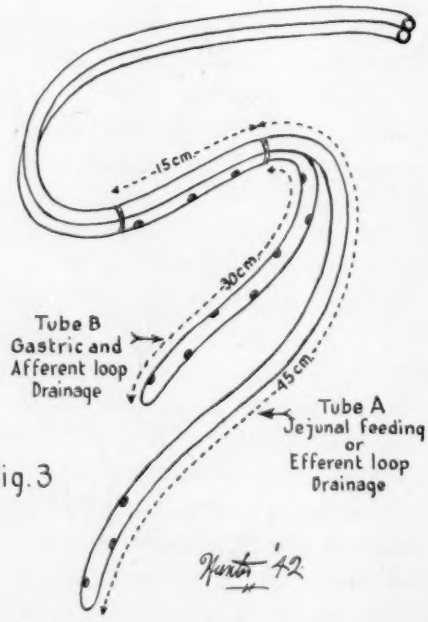

Fig. 3

The proximal ends are clearly labeled Feeding, on tube A, and Drainage, on tube B. This double tube is passed through the nose into the stomach prior to operation in the usual manner. To facilitate its passage the tip of tube B may be moored to tube A with black silk. Before completing the anastomosis tube A is passed 45 cm. into the efferent intes-

tinal loop, and tube B is passed 30 cm. into the afferent loop. No difficulty is encountered identifying the tubes because of the unequal length of their terminal tips. If aseptic anastomosis is to be performed a tube with a metal bucket may be substituted for tube A for identification.

On completion of the operation and return of the patient to his room, constant suction by means of a 3-bottle Wangensteen is applied to tube B for drainage of the afferent intestinal loop, and maintained for at least seventy-two hours. To insure patency of the tube and prevent occlusion of lumina, 10 c.c. of normal saline solution are instilled every hour. Suction drainage by this tube prevents distension of the afferent loop and guards against closed loop duodenal obstruction that Wangensteen has emphasized. By its added perforations it permits gastric drainage and prevents distension proximal to the anastomosis. Tube A is used for jejunal feeding or efferent loop drainage. Immediately upon return of the patient from the operating room jejunal feeding is begun in the form of a continuous drip regulated so that the patient will receive 1000 c.c. every eight hours. To this feeding may be added gastric and duodenal contents suctioned off by tube B. Jejunal feeding is continued for at least seventy-two hours and the patient is also permitted clear fluids by mouth as soon as desired. Additions are rapidly made and when the patient can take a well-balanced diet by the oral route, jejunal feeding is discontinued. Jejunal feeding may be interrupted and suction applied to this tube whenever it becomes necessary for intestinal decompression. Before the tube is removed it is clamped for a test period and if the patient's progress is satisfactory it is then withdrawn.

The advantages of early feeding to the debilitated patient are obvious. The patient receives nutrition with a carbohydrate, protein, and fat distribution that is impossible by the intravenous route; the danger of overloading the circulatory system is avoided, particularly in the old age group, which is often done when intravenous fluids are administered; additional medications may be introduced with facility through the jejunal tube.

SUMMARY

A simple double tube method for drainage and feeding following gastric resection or gastroenterostomy is presented. This method provides for constant and simultaneous gastric and afferent loop drainage. Early continuous jejunal feedings may be instituted. Discontinuing jejunal feedings provision is made for efferent loop decompression.

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THE POTENTIAL CLOSED DUODENAL LOOP IN GASTRIC RESECTION*

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THE occurrence of obstruction at the efferent outlet after gastrojejunal anastomoses is well known. Apart from a few reported instances of gangrene of the proximal afferent loop following gastrojejunal anastomoses, the occurrence of obstruction at the afferent inlet appears to have escaped the notice of surgeons as well as pathologists. In 1936, an instance of rotation of the proximal afferent jejunal loop with ensuant gangrene of the duodenojejunal loop, after an extensive resection for gastric carcinoma, was observed. The patient, Mr. C. B. (University Hospital No. 653763), died seventy-two hours after operation. The duodenum and afferent jejunal loop were distended and discolored. The serous surface of the bowel, in places, was torn. An antemortem blood culture as well as cultures taken from the peritoneal cavity and the bile in the gall bladder showed hemolytic streptococci.

In the intervening years, three additional patients have been seen, who came to autopsy presenting evidence of distention of the afferent duodenojejunal loop just proximal to the gastrojejunal anastomosis. In two of these, a gastric resection employing a retrocolic, Hofmeister plan of re-establishing gastrointestinal continuity had been done, in one instance for an obstructive duodenal ulcer, in the other, for gastric carcinoma. In the remaining patient, a posterior gastrojejunostomy had been made for a patient with a duodenal ulcer exhibiting high-grade pyloric obstruction. There was no suggestion of gangrene of the afferent duodenojejunal loop in any of these three patients, only distention of this loop without obvious cause. These three patients exhibited hyperthermia, tachycardia, and gradual decline of the blood pressure, followed by death within eighty hours after operation. The postoperative sequence of events was very much the same in each instance. The first two patients, in which this sequence of events obtained, were exceedingly poor risks and the finding of a patulous afferent inlet, despite the presence of a dilated proximal jejunal loop, persuaded the pathologists that this dilatation was without special significance. When, however, a third good-risk patient succumbed under similar circumstances, members of the surgical staff were convinced that such

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dilatation of the proximal duodenojejunal, afferent loop after gastric resection in the Billroth II type of operation was an item of real significance in the fatal issue.

The possibility of this occurrence has been mentioned previously, together with description of a technical maneuver to prevent its occurrence.[4, 7] It is the purpose of this paper to point out that: (1) Dilatation of the proximal duodenojejunal loop after gastric resection may be followed by hyperthermia, vascular collapse, and death without the occurrence of gangrene in the loop; (2) Experimental obstruction of the duodenojejunal loop in the dog is followed by the same sequence of events; and (3) This occurrence in man is probably infrequent but is a far more serious complication than obstruction at the efferent outlet. Placement of an indwelling duodenal tube within the afferent loop at the time of operation obviates this potential hazard.

CASE HISTORIES OF PATIETS DYING OF HYPERTHERMIA AND VASCULAR COLLAPSE DUE TO DISTENTION OF THE PROXIMAL DUODENOJEJUNAL LOOP

Summary of Case Histories.—Mr. S. J. S. (U. H. No. 695813), aged 59 years, in excellent physical condition, without obstruction, and with only slight weight loss, was operated upon for cancer of the stomach May 31, 1940. A Hofmeister retrocolic anastomosis with entero-anastomosis was made after excision of 85 per cent of the stomach. The operation, done under intratracheal cyclopropane anesthesia, was accomplished without incident. The lines of resection were found to extend beyond the microscopic boundaries of spread of malignancy. The patient's condition on return to the ward was good, the pulse being 80 and the systolic pressure 140 mm. Hg, the rectal temperature rose gradually to 106° F. and the pulse to 144 per minute (Fig. 1). The blood pressure declined and was difficult to sustain despite transfusion of adequate amounts of blood and plasma. Death occurred forty-eight hours after operation.

During the first twenty-four-hour period following operation, the oral intake was 250 c.c. During the same time 600 c.c. of a deeply bile-stained fluid were aspirated from the stomach. During the next twenty-four-hour period, 800 c.c. of fluid were ingested and 1,250 c.c. of a faintly bile-stained fluid was aspirated from the inlying gastric tube.

Permission for post-mortem examination was denied but examination of the peritoneal cavity through the abdominal incision immediately after death was allowed. The proximal jejunal loop was distended but appeared to have good color. It seemed to have become sharply angulated at the site of the gastrojejunal anastomosis. Both gastrojejunal stomas, as well as the entero-anastomosis, were patulous.

The other two patients, Mr. M. P. (U. H. No. 681414), aged 53 years, and Mrs. R. D. (U. H. No. 684265), aged 57 years, had been observed in this clinic at earlier dates. Both patients had been ill over many years with tuberculosis and duodenal ulcer. Both patients had been hospitalized in tuberculosis sanatoriums over long periods. One, Mr. M. P., had an active lesion at the time of hospitalization for duodenal ulcer. However, both patients were essentially afebrile prior to operation. Both patients, in addition, had high-grade duodenal obstruction and alkalosis from persistent vomiting. In each instance, the obstruction remained refractory to treatment on the medical service and the patients were transferred to the surgical service for operation. Both patients were operated upon without meeting adequately,

preoperatively, the caloric and nitrogen requirements of debilitated patients. In the instance of one, Mr. M. P., a posterior gastrojejunostomy was done; in the other, a Finsterer exclusion type of gastric resection was done with a Hofmeister retrocolic anastomosis. Both operations were done without special incident and in each instance the immediate recovery period was quite ordinary. Both patients had indwelling gastric duodenal tubes to which suction was applied.

After thirty-six hours, Mr. M. P. exhibited quickening of the pulse and elevation of temperature to 106° F. There was also auricular fibrillation and a drop in the blood pressure to shock level. The patient was bronchoscoped, it being believed that atelectasis was responsible for the unusual reaction. Death occurred seventy-nine hours after operation. Autopsy disclosed dilatation of the proximal duodenojejunal loop but there was no evidence of loss of viability. The gastrojejunal stomas were competent and patulous. There was no evidence of peritonitis. The lungs revealed an extensive active tuberculosis and also purulent bronchitis. The brain appeared normal, grossly; microscopic examination failed to disclose any significant finding. Apart from tuberculosis of the lungs, the only other important histologic finding was the observation of areas of liver necrosis. It was believed that the poor physical condition of the patient contributed largely to the fatal issue.

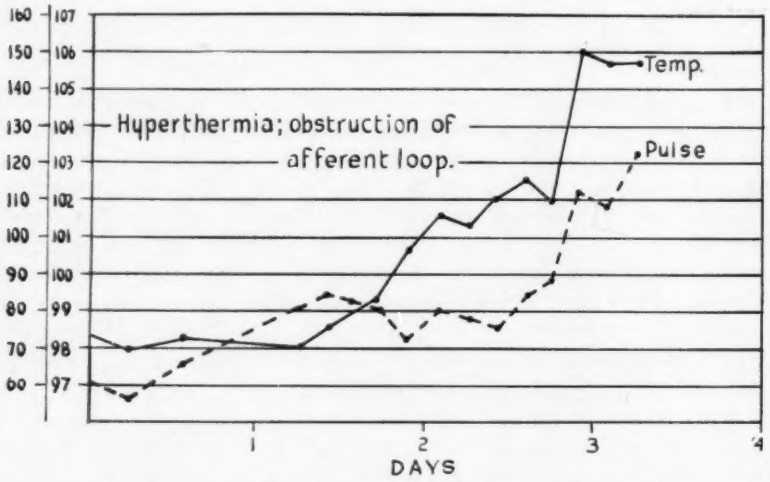

Fig. 1.—Hyperthermia attending obstruction of afferent gastrojejunal stoma in man.

The other patient, Mrs. R. D., exhibited a satisfactory convalescence for the first twenty-four hours, a pulse of 80 and a blood pressure of 130/80 having been sustained, with normal respiration. Following a chill, the temperature rose to 106° F. and the pulse accelerated to 120 beats per minute with a fall in blood pressure to 88/70. The patient remained in shock despite efforts to combat it. There were rales at the base of the right lung. Bronchoscopy was done without effect. Cyanosis deepened and tracheotomy was performed without improvement. The patient died thirty-nine hours after operation with hyperpyrexia, vascular collapse, and marked dyspnea. Autopsy disclosed extensive tuberculosis and bronchiectasis of the left lung. There was considerable edema of the right lung. There was an anomalous insertion of the bile duct into the duodenum. The liver was somewhat fatty. The proximal jejunal loop was distended, measuring 6 cm. in diameter. It contained a deeply bile-stained fluid. The loop appeared viable grossly. Microscopically the muscle was thin and somewhat fragmented. There were miliary abscesses in the portal spaces of the liver. Areas of the left lung exhibited fibrosis and the histologic findings of tuberculosis.

EXPERIMENTAL REPRODUCTION OF VASCULAR COLLAPSE AND HYPERTHERMIA SYNDROME IN DOGS ATTENDING ESTABLISHMENT OF A CLOSED DUODENAL LOOP

Method.—In thirteen dogs the following procedure was carried out. Under ether anesthesia and ordinary aseptic precautions, the duodenal loop was implanted subcutaneously in the manner of a Biebl skin-covered intestinal loop. Great care was observed not to injure the blood supply of the mobilized duodenal loop. Approximately ten days later, the duodenal loop was isolated by severing and inverting both ends. The experiment at this juncture being in the nature of an acute survival procedure, the continuity of the intestinal canal was not re-established.

The pressure in the loop was followed at intervals by introducing an 18 gauge needle through the skin directly into the subcutaneously implanted duodenal loop. The rectal temperature of the dog was recorded every four hours and he was allowed to wake up. In two animals, a No. 20 French urethral catheter was introduced into the distal end of the closed duodenal loop; in three dogs, a short closed duodenal loop, 10 to 15 cm. in length, was isolated, the bile and pancreatic ducts draining into the closed segment.

Results.—The results are summarized in Table I. It is to be noted that the survival time was considerably shorter than in the three patients noted above in whom only distention of the proximal duodenojejunal loop without obvious cause for the obstruction was noted. Fourteen of the animals showed an average maximum elevation of temperature of 105.2° F. In only one instance could the hyperthermia be explained on the basis of bronchopneumonia (Dog No. 17). In all instances save two (Dogs No. 9 and No. 17), the observed pressure in the closed duodenal loop exceeded that predicated by C. A. Dragstedt, Lang, and Millet (1929) to be necessary to arrest venous return from the duodenum. The average time intervening between observation of the critical duodenal intraluminal pressure noted by Dragstedt and his associates (see Fig. 3) and death of the animal was approximately fifteen hours.

The protein content of the peritoneal fluid was determined in a number of instances. It was invariably high. Values ranging from 4 to 6 Gm. per cent were usual, indicating that markedly increased capillary permeability was present. However, we were rather surprised to note that when a catheter was attached to a small fenestrated glass tube and placed in the peritoneal cavities in unobstructed dogs and cats, a peritoneal fluid with a high protein content was obtained, also. Usual values in these instances were concentrations of protein in the peritoneal fluid of 2.5 to 5 Gm. per cent.

DISCUSSION

That closed duodenal loops develop high intraluminal pressures is well known. Morton and Sullivan (1930) isolated closed intestinal

TABLE I

EFFECTS OF CLOSED DUODENAL LOOPS IN THE DOG

DOG NO.	LENGTH OF LOOP	MAXIMUM PRESSURE CM. H_2O	TIME OF MAXIMUM PRESSURE (HR.)	MAXIMUM TEMPERATURE	TIME OF MAXIMUM TEMPERATURE (HR.)	SURVIVAL (HR.)	CONDITION OF LOOP	MISCELLANEOUS
1	Entire duodenum	35 to 36.5	11	104.6	12½	14	Loop intact, distended necrotic at antimesenteric border	Liver soft, friable, and congested
2	Entire duodenum	57 to 58	9	106.0	11½	12½	As above	As above
3	Entire duodenum	27 to 40	5½	103.6	7½	12	Intact, no distention, no gangrene	As above
4	Entire duodenum	33 to 78	12	104.4	4½	52	Intact, distended, necrotic at antimesenteric border	As above
5	Entire duodenum	54 to 58	9½	103.2	10½	18	Not intact, gangrene with perforation at distal end	Peritonitis
6	15 cm.	68.5	8	106.4	22	24	Intact, distended, necrotic at antimesenteric border	Liver soft, friable and congested
7	15 cm.	65 to 68	35	106.4	34	46	As above	As above
8	Entire duodenum	47 to 54	8½	101.4	7	10½	As above	As above
9	Entire duodenum	None	None	99	14	15	As above	Peritonitis
10	Entire duodenum	64 to 78	12	104.7	6½	30½	As above	Liver soft, friable and congested
11	Entire duodenum	62	10	105.8	29½	40	As above	As above
12	Entire duodenum	48	2	104	7	9	As above	As above
13	10 inches	42	2	101.6	14½	22	Perforated at distal end at antimesenteric border	Peritonitis
14	Entire duodenum	41	18	107.4	23	23	Necrotic at antimesenteric border; intact and distended	Liver soft, friable and congested
15	Entire duodenum	22	9	105.4	16	16½	As above	As above
16	Entire duodenum	36 to 60	10½	101.5	12½	12½	Open at distal end, no gangrene	Peritonitis
17	Entire duodenum	None	None	105.4	24	24½	Intact, distended, necrotic at antimesenteric border	Bronchopneumonia
18	Entire duodenum	50 to 95	24	105.4	54	57	As above	Liver soft, friable and congested

loops 10 cm. in length in the ileum and duodenum, into which the biliary and pancreatic secretions did not drain. They noted that the intraluminal pressure and the amount of secretion in the closed duodenal loops far exceeded that of the closed ileal segments. That dogs with closed duodenal loops into which the biliary and pancreatic secretions drain, die with symptoms of vascular collapse and hyperthermia in just the same manner as may attend obstruction of the proximal afferent, duodenojejunal loop after the Billroth II type of operation in man, is significant. Inasmuch as the obstruction is complete in the dogs, it is understandable that the survival time is shorter than in the fatal instances observed after operation upon man. Harms (1927) observed, in cannulating the common bile duct and the main pancreatic duct in the dog, that secretion continued until pressures of 376 to 460 mm. of pancreatic juice and 309 mm. of bile were reached. Herring and Simpson (1906) observed secretory biliary pressures of 300 to 350 mm. of water. In short closed duodenal loops from which both biliary and pancreatic secretions were excluded, Morton and Sullivan observed secretory pressures of 300 to 370 mm. of water regularly. In one instance, the secretory pressure mounted to 520 mm. of water.

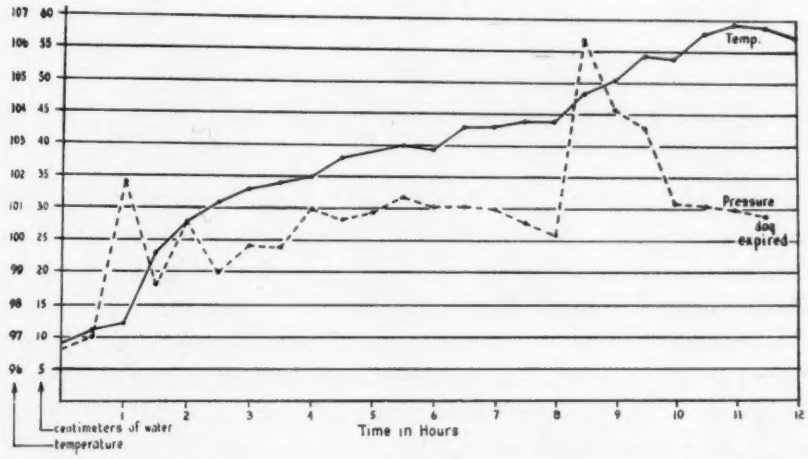

Fig. 2.—Hyperthermia attending closed duodenal loop obstruction in the dog (Table I, Dog 2). The intraluminal pressure in the obstructed segment is indicated also.

Apart from the greater secretory pressures present in the duodenum, there is another item which makes this segment of the gut more susceptible to injury through the agency of increased intraluminal pressure than segments of ileum or colon. C. A. Dragstedt, Lang, and Millet (1929) have indicated that the manner of penetration of the circular muscle coat of the bowel by the mesenteric vessels differs considerably in various segments of the bowel. Ochsner and Storck (1937) have shown in a graphic manner, how a relatively small intraluminal pressure will obliterate the venous outflow from the duodenum, whereas far greater pressures are necessary to retard venous outflow from the colon (Fig. 3).

How obstruction of the afferent duodenojejunal loop comes about in man after gastric resection is not easy of appraisal. Elsewhere,[8, 9] it has been pointed out that obstruction at the efferent outlet in man after gastrojejunal anastomosis, comes about largely through the agency of overinversion of tissue by the surgeon. In the experience of this clinic, this is probably *the sole* cause of obstruction at the efferent outlet. It is very unlikely that such items as whether the proximal loop is iso- or antiperistaltic in direction with reference to its attachment to the stomach, whether it is short or long, what direction the incision in the gastric wall takes for the anastomosis—these factors are probably all

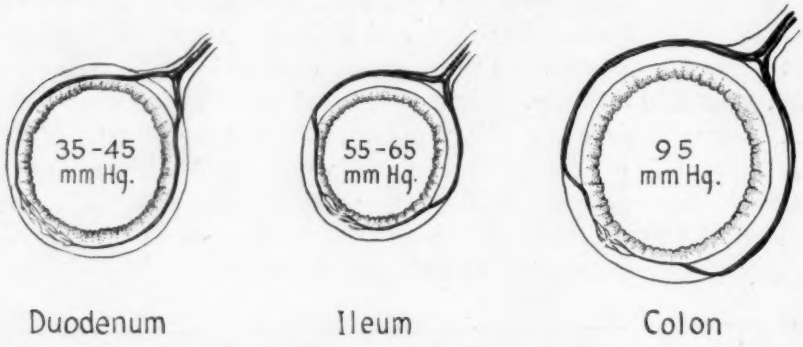

Fig. 3.—Venous obliteration attending intraluminal pressure at various levels in the bowel. Owing to the immediate penetration of the muscular coat by the vessels, at the mesenteric border (5 and 7 o'clock), relatively small increases of intraluminal pressure will cause venous obliteration as contrasted with the colon, where the entry of the vessels is at 1 and 11 o'clock. In the ileum, the vessels enter at 3 and 9 o'clock. (Redrawn from Ochsner and Storck.)

inconsequential as far as the development of obstruction at the efferent outlet is concerned. The only thing that matters, apart from *fixing* the gastric stoma *below* the transverse mesocolon as Polya has emphasized in retrocolic anastomosis, is that the surgeon approximate a *minimal* amount of the adjacent walls of the stomach and jejunum in making the anastomosis. The experience of this clinic suggests that .5 to .75 cm. of the adjacent gastric and jejunal walls suffice to establish a satisfactory anastomosis (Fig. 4).

The most likely cause of obstruction, at the afferent outlet, on the contrary, is sharp angulation or kinking of the loop. And, unfortunately, as the recital of the cases mentioned in this report indicates, incomplete occlusion may bring about a fatal issue.

It is for this reason that we have come, in this clinic, to employ an indwelling duodenal tube extending into the proximal afferent inlet loop as a matter of routine in gastrojejunal anastomoses. In all probability, this complication of angulation at the afferent inlet does not occur often, yet, when it does occur, it is usually fatal. Maintaining the afferent channel widely patulous by the placement, at operation, of a fork of an indwelling duodenal tube into this limb of the gastrojejunal anastomosis assures continuity of this important channel.

Following observation of the instance of frank gangrene of the proximal duodenojejunal loop after gastric resection for carcinoma of the stomach in this clinic in 1936, it became routine practice for several years thereafter, to add an entero-anastomosis regularly in all resections for gastric malignancy. It is to be noted that, in the fatal issue reported

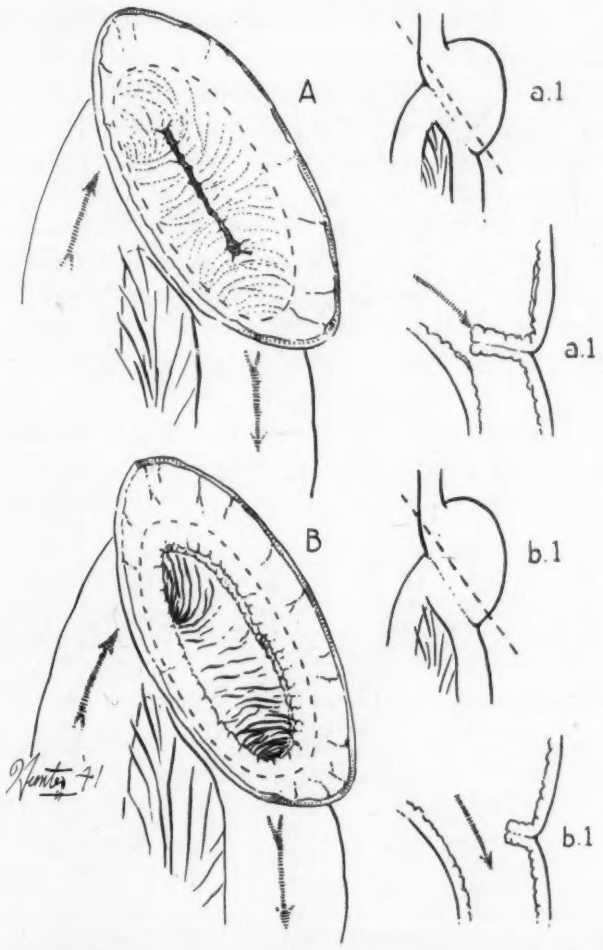

Fig. 4.—Mechanism of obstruction at the efferent outlet after gastrojejunal anastomoses. *A*, Inversion of too much tissue creates a flap, which obstructs at the efferent outlet; obstruction at the afferent inlet through such an agency is distinctly unusual. *B*, The gastrojejunal stoma after incorrect and correct suture. *a.1*, Oversuturing (incorrect) with narrow stomal slit and obstructing flap at efferent outlet. *b.1*, Wide stomal slit with large patulous stomas at inlet and outlet (correct), after inversion of .5 cm. of the adjacent gastric and jejunal walls in the anastomosis. (Medico-Surgical Tributes to Harold Brunn, San Francisco, University of California Press, 1942.)

here in the good-risk patient in which hyperthermia developed, an entero-anastomosis had been made and bile was obtained by suction from the inlying gastric tube, and yet distention of the proximal duodenojejunal loop occurred followed by death of the patient.

During recent years, all resections of the alimentary canal in this clinic, including gastric resections, have been made by the closed method. It is obviously a frank break in the aseptic technique to pull a straight

or forked catheter out from the residual gastric pouch through the gastrojejunal stoma in order to place the catheter or both limbs of a forked catheter into the afferent and efferent jejunal loops. Nevertheless, the experience of this clinic, with a large number of gastric resections for both ulcer and malignancy, suggests that this is an important expedient in obviating a potentially serious complication (Fig. 5).

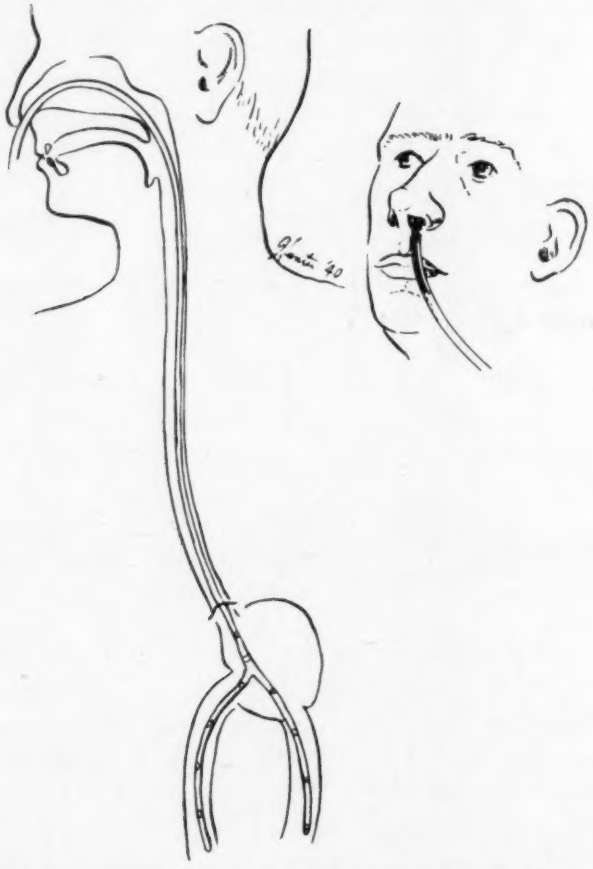

Fig. 5.—Forked catheter employed to prevent obstruction in the proximal jejunal loop after gastrojejunal anastomoses; one limb of the catheter is placed in the distal jejunal loop as well. Suction can be exerted simultaneously on the residual gastric pouch, the afferent and efferent limbs. A straight tube with multiple perforations inserted into the afferent loop meets the situation quite satisfactorily too. The tube is removed seventy-two hours after operation. (Surg. Gynec. & Obst. 72: 257, 1941.)

The safety of an operation depends upon leaving little to chance. Obstruction at the afferent inlet probably does not happen often and the causes which may provoke it are not entirely clear. On completion of the retrocolic antiperistaltic short-loop, Hofmeister gastrojejunal anastomosis, it is not uncommon to see the afferent loop assume a rather bizarre position, even with the transverse mesocolon anchored carefully to the stomach 1 cm. above the stoma. It affords the surgeon much comfort to know that a catheter in that loop will keep the duodenojejunogastric channel open during the early postoperative period.

SUMMARY

A syndrome of hyperthermia, vascular collapse, and death is described attending distention and partial obstruction without gangrene of the proximal duodenojejunal loop after gastric resection. Three cases are cited in which it is believed that distention of the proximal duodenojejunal loop was directly responsible for the fatal outcome.

When a complete closed loop obstruction is established in the duodenum of the dog, high secretory pressures ensue. Necrosis of the bowel is a regular accompaniment and perforation and gangrene are observed not uncommonly. The survival time is far shorter than that noted in man with distention occasioned by incomplete obstruction of the afferent duodenojejunal loop. Hyperthermia and vascular collapse attend, also, the closed loop duodenal obstruction of the dog. Death, in both man and dog, is owing, no doubt, to increased capillary permeability consequent upon a damaged bowel wall. Bacteria may migrate through the bowel wall to the peritoneal cavity or reach the liver via the duodenal veins.

The mechanism of obstruction at the afferent inlet after gastrojejunal anastomoses is not entirely clear. However, an effective means of preventing this unusual but serious potential postoperative complication is described.

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THE TREATMENT OF ACUTE APPENDICITIS IN CHILDREN AS INFLUENCED BY CHEMOTHERAPY

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INTRODUCTION

SINCE the publication by Domagk,[1] 1935, dealing with the effects of prontosil on streptococcus infections in mice, treatment of such infections in man by chemotherapy or sulfonamide drugs has progressed rapidly. While in general a maximum therapeutic effect on some particular organism has been associated with a particular compound, evidence has accumulated to prove that the effective coverage of most of the compounds is wide enough to include a number of organisms. This is particularly true for those organisms associated with peritonitis secondary to appendicitis; namely, streptococcus, *Bacillus coli, B. welchii,* and certain other anaerobes. Infections in animals due to all these organisms have been shown to be influenced favorably by sulfanilamide, sulfapyridine, and sulfathiazole. These three drugs have been utilized as an aid to surgery in the treatment of appendicitis and its complications at the St. Louis Children's Hospital during the past four years. This paper is presented to show the results of such treatment. A comparison of the results in this period is made with those of a previous period of fifteen years' duration.

Others also, including Ravdin, Rhoads, and Lockwood,[2] 1940, Long and Dees,[3] 1941, and Thompson, Brabson, and Walker,[4] 1941, have reported improved results in the treatment of peritonitis associated with appendicitis through the use of the sulfonamide drugs.

GENERAL CONSIDERATIONS IN CHEMOTHERAPY

Most observers believe that the action of the sulfonamide compounds is one of growth inhibition or bacteriostasis. The newer drugs are capable of holding the invading organisms in check until antibodies are developed sufficiently to bring about bacteriolysis. A lag period of four to six hours has been shown to exist before the maximum effectiveness of the drugs becomes manifest.

It is our practice to administer the drugs prior to operation in all cases of appendicitis where peritonitis is diagnosed or even suspected. Experience has demonstrated that it is in the invasive stage, not in the chronic or entrenched stage, that chemotherapy is most effective. This is the basis for the belief that there is less danger in operating on patients with peritonitis than formerly, provided an effective drug is used

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before, during, and for a limited period after the operation. There is no longer the great danger of a disastrous spread of the infection by operative procedures. It must be emphasized that chemotherapy in itself cannot be maximally effective where there is a continuing addition of infectious organisms or when pus is present in walled-off abscesses. Long-continued use of the drugs with delay in surgical drainage of abscesses is not only useless but actually may be harmful. In acute infections the drugs must be administered in sufficient amounts to bring quickly the concentration in the blood up to levels which have been found effective. The choice of drug dosage and administration intervals used by us is the result of extensive research by Hartmann and his associates,[5] 1940, on chemotherapy.

DOSAGE

The blood levels found effective for sulfanilamide range from 8 to 14 mg. per cent, for sulfapyridine and sulfathiazole, 6 to 12 mg. per cent. To reach such levels quickly, 1.0 per cent sulfanilamide in normal saline solution, or a 5 per cent solution of the sodium salts of sulfapyridine or sulfathiazole, is given intravenously. Sulfanilamide, sulfapyridine, and sulfathiazole are administered on the basis of 0.2 Gm. per kilogram body weight in six divided doses. Sulfanilamide can be administered subcutaneously on the basis of 0.1 Gm. per kilogram body weight given twice a day in the form of an 0.8 per cent solution. When sodium sulfapyridine is given intravenously the dosage is 1 c.c. of the 5 per cent solution per kilogram body weight repeated every eight hours; for sodium sulfathiazole 2 c.c. of 5 per cent solution per kilogram body weight every six hours, as it is excreted much more rapidly. Occasionally 2 to 5 Gm. of sterilized powdered sulfanilamide have been placed locally in an abscess cavity or in the area from which an adherent gangrenous appendix has been removed, or in the muscle layer during closure in an infected or potentially infected appendix.

COMPLICATIONS

Complications from the use of the drugs in children are not severe or frequent. Nausea and vomiting develop in some patients. Usually during the period when the concentration of the drug must be maintained at a high level, gastric suction is also used, which tends to eliminate vomiting. In a few patients the dosage may have to be decreased to stop vomiting. In our series of cases no severe leucopenia or anemia has resulted. The presence of a leucopenia from a severe infection prior to treatment has not been a contraindication to the use of drugs. Renal bleeding occasionally is met with and usually is relieved by changing to another drug or lessening the amount of the drug being administered. In severely toxic patients, jaundice has followed the use of the drugs in a few cases. Cyanosis due to elevated methemoglobin concentration is often encountered. This can be counteracted by the intravenous ad-

ministration of methylene blue, using 1 to 2 mg. per kilogram body weight, or by the giving of 1 to 2 gr. every four hours as needed by oral route. It is deemed especially advisable to give methylene blue preoperatively at least one hour before an anesthetic. To help in the recognition of toxic effects of the drugs, daily blood studies, urinalysis, and methemoglobin determinations are done.

EFFECTS OF CHEMOTHERAPY

The beneficial effects attributable to chemotherapy in the treatment of the complications of appendicitis in children are: (1) a rapid lessening of the toxicity, (2) a rapid regression of the peritonitis, (3) a reduction in the number of cases requiring drainage, and (4) a shortening of the period of illness. The added effect has been practically to eliminate death as a sequel to peritonitis associated with appendicitis. Even though it is acknowledged that chemotherapy has improved greatly the prognosis in appendicitis, properly instituted surgery still plays the most essential role. The earliest possible removal of the source of continuing contamination of the peritoneal cavity is imperative. Chemotherapy alone cannot and should not be relied upon to cure infection of the peritoneal cavity from a gangrenous or ruptured appendix.

PREOPERATIVE CONSIDERATIONS

It is well recognized that before any operation is performed the fluid, electrolytic and nutritional deficiencies or derangements of the patient must be corrected. Protracted nausea and vomiting may be assumed to indicate a food and electrolytic deficiency. From blood studies, the hematocrit reading, blood chloride and plasma protein determinations, a more precise knowledge of these deficiencies can be procured.

The steps necessary to correct a loss of fluid and electrolytes are well known. In children the dosage of Ringer's solution is usually 50 to 60 c.c. per kilogram body weight, given subcutaneously; 20 to 30 c.c. of 10 per cent dextrose per kilogram body weight can be given intravenously to overcome food deficiency. It can be added to Ringer's solution when given intravenously or separately. Protein deficiency can be corrected by the administration of plasma, 30 c.c. per kilogram body weight. If plasma is not available casein digest in the form of a 5 per cent amino acid mixture with 10 per cent dextrose may be substituted (Elman,[6] 1940). A child requires 2.5 Gm. of protein per kilogram body weight per day, the mixture given intravenously.

Usually two to six hours are required to prepare the patient for operation and if the case is severely toxic eight to twenty-four hours may be necessary.

OPERATION

During the operation, especially in toxic cases, the anesthetic must be administered carefully. Drop ether is employed. The patient is kept

as light as possible and cyanosis is avoided. In severely toxic cases an attempt is often made to open the abdomen under local anesthesia. Ether then is administered to permit adequate exposure to complete the operation quickly. *The appendix should always be removed.* Drainage is used only if abscess formation has injured the peritoneum locally. It is not used if the peritoneum is involved to the same degree diffusely. Chemotherapy makes the use of drains less frequently necessary. This, in turn, results in fewer instances of postoperative obstruction due to adhesions.

The operation usually is done through a low right rectus incision with retraction of the muscle in clean cases or splitting of the muscle in contaminated cases. The McBurney incision seldom is used unless a definitely localized abscess is present.

POSTOPERATIVE CARE

Postoperative chemotherapy is continued at a high level until the temperature subsides. This happens much sooner under such treatment than in those cases not treated with chemotherapy. Intravenous fluids, electrolytes, and nutritive substances are favored immediately after operation rather than the early administration of food by mouth. After the temperature subsides the drug is continued at one-half the previous dosage for three to five days. In all other respects the practices followed are those in general use.

ILLUSTRATIVE CASES

CASE 1.—An acutely ill boy, 4½ years old, was admitted to the St. Louis Children's Hospital, Aug. 13, 1940. There was a history of abdominal pain, nausea, and vomiting of two days' duration. An enema had been given but no cathartic. Temperature at the time of admission was 38.1° rectally; respirations, 28; and pulse, 160. The skin was hot and dry, nasopharynx and chest findings were negative. Abdominal examination showed the child's legs drawn up as if in pain, with marked rigidity and localized tenderness below and to the right of the umbilicus. Definite rebound tenderness was present. Rectal examination was negative; urine, negative; W.B.C., 25,000.

A diagnosis of acute appendicitis with probable peritonitis was made. The patient was given 30 c.c. of 5 per cent sodium sulfathiazole intravenously (1.5 Gm.), as well as 200 c.c. of 10 per cent glucose intravenously, and 200 c.c. Ringer's solution subcutaneously. Four hours later the child was operated upon under drop ether anesthesia. The appendix was gangrenous in its distal third. Within the abdominal cavity a creamy exudate was encountered, which on culture revealed *B. coli.* The appendix was removed and the abdomen closed without drainage. Postoperatively, sulfathiazole and fluids were continued. On the third postoperative day the temperature was normal and the patient was on a soft diet. The wound healed by primary intention and the patient was discharged on the ninth postoperative day.

CASE 2.—A four-year-old colored girl was admitted April 20, 1940. There was a history of pain in the abdomen, nausea, and vomiting of four days' duration. The child had been given castor oil. Prior to entry the pain and vomiting became worse, the child became distended and drowsy. Temperature on admission, 38°

C.; respirations, 32; pulse, 126. Examination revealed a markedly toxic patient with a dry skin. The pharynx and chest findings were negative. The abdomen was distended markedly, dullness was present in the flanks, no sounds could be heard on auscultation, and some generalized tenderness was present. The white blood cell count was 5,200; urine, negative.

A diagnosis of acute appendicitis with peritonitis was made. Wangensteen suction was instituted; intravenous and subcutaneous fluids were given. One gram of 1 per cent sulfanilamide in Ringer's solution was administered subcutaneously every four hours, or .4 Gm. per kilogram body weight per twenty-four hours. Twenty-four hours later operation was performed under drop ether anesthesia. When the peritoneum was opened there was a gush of foul-smelling pus and loops of ileum were found covered with a thick fibrinous purulent exudate. The appendix was lying free and had amputated itself at the base. The appendical stump was open. This stump was closed, drains were placed, and the abdomen was closed.

Nasal suction was instituted postoperatively. The child was given intravenous fluids, glucose, methylene blue, blood transfusions, vitamins and 1 per cent sulfanilamide subcutaneously. The sulfanilamide concentration the day following the operation was 24.6 mg. per cent. At this time the child was more alert and the temperature curve was starting downward. The nasal tube was removed on the third postoperative day, and the patient began taking broth and tea. On the sixth postoperative day the child was on a soft diet and was discharged as well, May 16, 1940.

CASE 3.—A white girl, 8 years old, was admitted Dec. 4, 1940, with a history of cramping abdominal pains, fever, chilly sensation, watery diarrhea and persistent vomiting of four days' duration. On entry to the hospital the child was restless and lethargic. She was markedly dehydrated and toxic. Temperature on admission, 38.8° C.; respirations, 42; pulse, 120. The color of the patient was dusky. The pharynx and lungs were clear. The right abdomen was diffusely tender and rigid; W.B.C., 22,000; urine, negative; and vaginal smear showed no pneumococci. Blood culture showed no growth.

The child was given fluids intravenously. Five per cent sodium sulfapyridine was administered intravenously every eight hours. After sixteen hours of observation and therapy the condition did not improve, even though the blood sulfapyridine determination was 11.3 mg. per cent.

A clinical diagnosis of peritonitis, the type undetermined, was made. Since the source might be a perforated appendix, an exploratory laparotomy was advised. This was done under local anesthesia, the child being very toxic and difficult to arouse. When the abdomen was opened, considerable congestion and edema of the appendix and intestines were found. Much fibrin and thick pus were present. A smear made immediately showed diplococci. These were identified subsequently as type one pneumococci. No Meckel's diverticulum was found. The appendix was removed and the abdomen closed without drainage.

Postoperatively, the patient was continued on sodium sulfapyridine. She was placed in an oxygen tent. Fluids and glucose were given intravenously; multiple transfusions were administered. On the fifth postoperative day she was taken out of the oxygen tent and was given fluids and medication by mouth. On the sixth postoperative day she developed a right lobar pneumonia followed by an empyema which later required drainage. She was discharged as well on Jan. 21, 1941.

This case while not one of appendicitis is presented because idiopathic peritonitis is differentiated, often with difficulty, from peritonitis secondary to appendicitis. The course followed in this case is the one recommended by us in all cases of peritonitis of doubtful origin. Exploratory

operation through a small incision is recommended rather than needling, because by the latter method fluid is not always obtained, and if fluid containing streptococci is obtained, the appendix still may be the primary cause of the disease. If the exploration reveals appendicitis the wound is enlarged to permit appendectomy, if not, the appendix usually is not removed.

STATISTICAL DATA

During the past four years, 1938-1942, at the St. Louis Children's Hospital there have been 223 appendectomies, or operations for appendicitis, with five deaths, a mortality of 2.2 per cent.

It is to be noted that no deaths occurred following operations for acute unruptured appendicitis, recurrent unruptured appendicitis, or acute

TABLE I

MORTALITY FOR DIFFERENT TYPES OF APPENDICITIS

(JANUARY, 1938, TO JANUARY, 1942)

TYPE	NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)
Acute, unruptured	102	0	0
Recurrent, unruptured	75	0	0
Acute, local peritonitis	14	0	0
Acute, diffuse peritonitis	32	5	15.6
Total	223	5	2.2

TABLE II

MORTALITY RATE ACCORDING TO CLASSES (1915-1932)

CLASS	TOTAL CASES	DEATHS	MORTALITY (PER CENT)
1	21	0	0
2	31	0	0
3	65	1	1.56
4	99	2	2.02
5	122	11(a)	9.02
6	42	16(b)	38.10
Total	380	30(c)	7.89

Appendicitis according to classes: (1) chronic, (2) recurrent, (3) subacute, (4) acute unruptured, (5) ruptured with abscess, (6) ruptured with peritonitis.
Letters (a), (b), and (c) denote the inclusion of one, two, and three patients, respectively, who died without operation.

TABLE III

AGE INCIDENCE IN RELATION TO MORTALITY

(JANUARY, 1938–JANUARY, 1942)

AGE (YR.)	SIMPLE APPENDICITIS (NUMBER OF CASES)	MORTALITY (PER CENT)	APPENDICITIS COMPLICATED (NUMBER OF CASES)	DEATH	MORTALITY (PER CENT)
1 to 3	5	0	5	2	40
3 to 6	14	0	9	2	22
6 to 9	31	0	8	1	12
9 to 12	69	0	14	0	0
12 to 15	58	0	10	0	0
Total	177	0	46	5	10

TABLE IV

ANALYSIS OF FATAL CASES

ADMISSION DATE	AGE (YR.)	DURATION OF ILLNESS (IN DAYS) BEFORE TREATMENT	PREOPERATIVE CHEMOTHERAPY	OPERATION	POSTOPERATIVE CHEMOTHERAPY	DATE OF DEATH	CAUSE OF DEATH
3/16/38	7	2	Adequate	Exploratory laparotomy; appendix not removed	Adequate	3/28/38	Peritonitis
7/25/38	2	8	None	Appendectomy	Very inadequate	7/26/38	Peritonitis
1/ 6/39	3½	8	Adequate	Exploratory laparotomy; appendix not removed	Adequate	1/15/39	Peritonitis
5/17/39	2	5	Adequate	Appendectomy with drainage	Adequate	7/16/39	Intestinal obstruction
7/25/39	3	2	None	Appendectomy	None	7/25/39	Death during operation. Anesthesia (?), peritonitis

appendicitis with local peritonitis. The five deaths which occurred resulted from appendicitis associated with diffuse peritonitis. There were thirty-two cases of diffuse peritonitis, making the mortality rate 15.6 per cent. During 1940 and 1941 there were no deaths at the St. Louis Children's Hospital from appendicitis or its complications. It was during this period that the principles governing the treatment of appendicitis, as outlined above, first were employed unfailingly.

In Table II are shown the results in cases of appendicitis during a previous period, 1915-1932, at the Children's Hospital as summarized by E. L. Keyes,[7] 1934. Note a total mortality of 7.89 per cent instead of the present 2.2 per cent and a mortality of 38 per cent as compared to the present 15.6 per cent for cases with ruptured appendicitis with diffuse peritonitis.

In Table III the age incidence in relation to mortality is shown.

In Table IV an analysis of the five fatal cases during the 1938-1942 period is presented. The analysis indicates that peritonitis is the usual cause of death following appendicitis. It is felt definitely that the involved appendix should be removed. Inadequate exposure is often the only factor which prevents this.

SUMMARY

During the past four years at St. Louis Children's Hospital the mortality from acute appendicitis and its complications has been reduced from a previous average of 7.89 per cent to 2.2 per cent.

The improved results are ascribed essentially to the early removal of the appendix, to intensive and well-directed pre- and postoperative care, and to the adequate use of the sulfonamide drugs before and after operation.

During 1940 and 1941 there were no deaths from appendicitis.

The methods of administration of the sulfonamide drugs and the surgical principles governing the care of patients before and after operation are described.

The authors wish to express their appreciation to Dr. A. F. Hartmann and his associates for the cooperation of the medical service in this problem of appendicitis.

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REPORT OF A CASE OF UNUSUAL ANOMALY OF THE BILE DUCTS IN AN ADULT WITH OBSTRUCTIVE JAUNDICE

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THIS case is of interest chiefly because of the unusual anomaly of the bile ducts found at operation and the technical difficulties and dangers incidental to this anomalous arrangement. The case also presents certain points of diagnostic interest.

The patient is a female, aged 51 years, who was admitted to the Hamilton General Hospital on April 7, 1940.

Past History.—She has had flatulent dyspepsia for twenty years. Nine months before admission she had an attack of indigestion which was followed by jaundice lasting two to three weeks. Another similar attack occurred three months before admission and again three weeks before admission.

The jaundice following the last attack persisted and increased until her entry into the hospital. She states that she had some epigastric discomfort in these attacks but no pain. She had lost twenty pounds in weight during the nine months previous to entering the hospital.

Complaints.—On admission, Mrs. M. complained of weakness, loss of weight, and jaundice.

Physical Findings.—Jaundice was very marked and was of the orange type. Stools were clay colored and the urine was dark. The liver was palpable one and one-half inch below the costal margin and was smooth. The gall bladder could not be palpated and tenderness was absent. The spleen was not palpably enlarged.

Laboratory Findings.—Urine showed ++ bile; stools also showed traces of bile at times. Van den Bergh's test was direct +, indirect ++++; icterus index was 99 on April 10, and gradually fell to 54 on April 25. Fragility test was normal and galactose tolerance test showed an excretion of 2 Gm.

X-ray Examination.—Flat plate and gastrointestinal series were negative. Because of the jaundice, iodeikon was not used.

Discussion of Diagnosis.—Parenchymatous disease was ruled out by the galactose tolerance test and the absence of an enlarged spleen. Hemolytic jaundice was excluded by the normal fragility test.

Carcinoma of the head of the pancreas was excluded by the absence of an enlarged gall bladder, the fact that the jaundice was not extreme, was not complete, and was diminished rather than increased.

Stone in the common duct was suspected because of the long history of flatulent indigestion in spite of the absence of definite pain preceding the onset and laparotomy was advised.

Preoperative Preparation.—Vitamin K and bile salts were given until the prothrombin time was normal and fluids and glucose were administered freely.

Operation.—The gall bladder lay in its normal position attached to the under surface of the liver. It was distended and shaped somewhat like a dumbbell, consisting of two globular distended portions connected by a narrow waist. The lower pouch of the gall bladder contained a hard mass and was entirely covered by the peritoneal fold of the hepatoduodenal ligament (Fig. 1).

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This overlying peritoneal fold was divided and reflected and dissection was carried out to expose the cystic hepatic and common bile ducts. A large duct was found entering the distended lower pouch of the gall bladder. This duct was three-eighths of an inch in diameter and as it passed down behind the duodenum was obviously the common duct (Fig. 2). No evidence of a cystic duct could be found. The fundus of the gall bladder was separated from the liver above and dissection was carried downward. The cystic vessels were encountered and ligated and another duct coming from above was found entering the distended lower pouch of the gall bladder on its upper aspect. This duct was about five-eighths of an inch in diameter (Fig. 3). The gall bladder was then opened to make sure we were not dealing with a densely adherent common duct (Fig. 5). A mass of small gall stones cemented together with puttylike material was removed from the distended

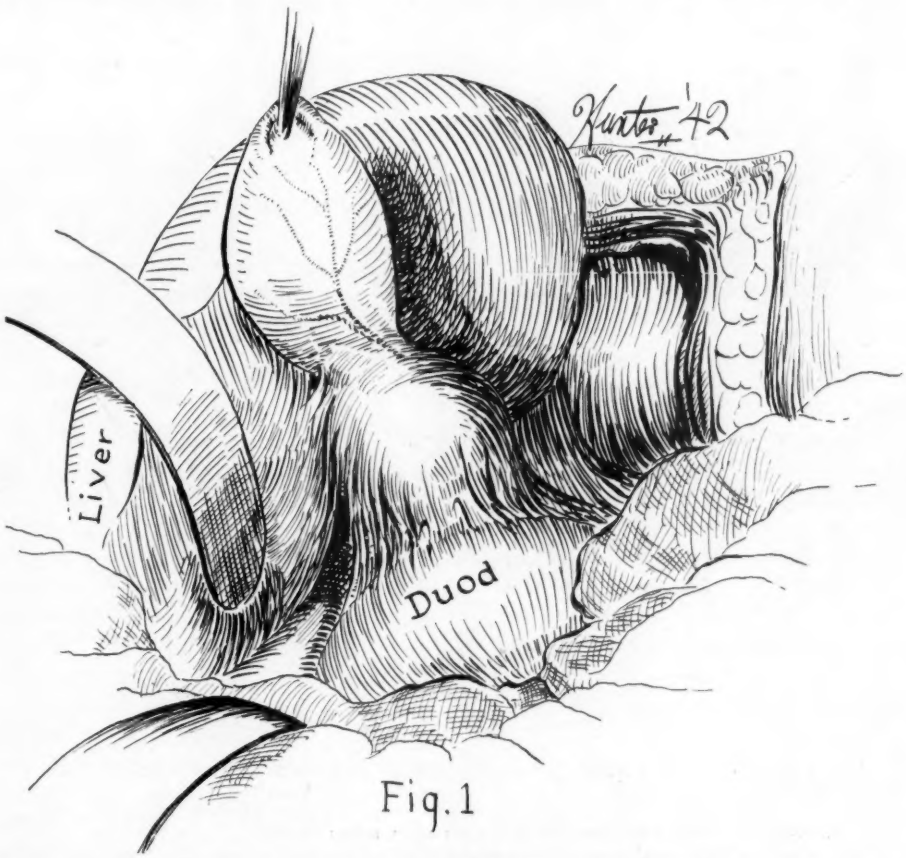

Fig. 1.—Condition seen on exposing the gall bladder; note the distended lower pouch enveloped by the gastrohepatic ligament.

lower segment. The orifices of both ducts displayed by dissection could be seen from within the gall bladder and a probe was passed into these ducts. No other orifice could be found. The gall bladder formed the only connection between the common hepatic duct and the common bile duct, the cystic duct being absent (Fig. 6). We then had the following three alternatives: (1) Cholecystostomy; (2) partial resection, leaving the lower segment of the gall bladder; (3) complete cholecystectomy with subsequent anastomosis of the ducts (Fig. 7).

We chose the latter procedure, that is, uniting the ducts over a T tube. The tube was left in situ for several months and the patient has had no trouble since.

Specimen.—The specimen is a thick-walled gall bladder with two orifices at its lower end where the ducts were divided (Fig. 8). The ducts were divided as near the gall bladder as possible, leaving no stumps on the latter in order to preserve as much duct as possible for approximation. There was no segment of duct attached to the gall bladder, thus ruling out the dreaded possibility shown in Fig. 5.

Pathologic Report (Summary).—The gall bladder showed adhesions and two openings, one labeled "hepatic duct" measuring 0.7 cm. and the other labeled "common duct" measuring 0.3 cm. The wall was thick and tough and the contents consisted of numerous facetted calculi which were irregular in shape and were imbedded in soft friable material.

Microscopic examination showed the mucosa to be infiltrated with chronic inflammatory cells and the subjacent tissue to be edematous and densely fibrous.

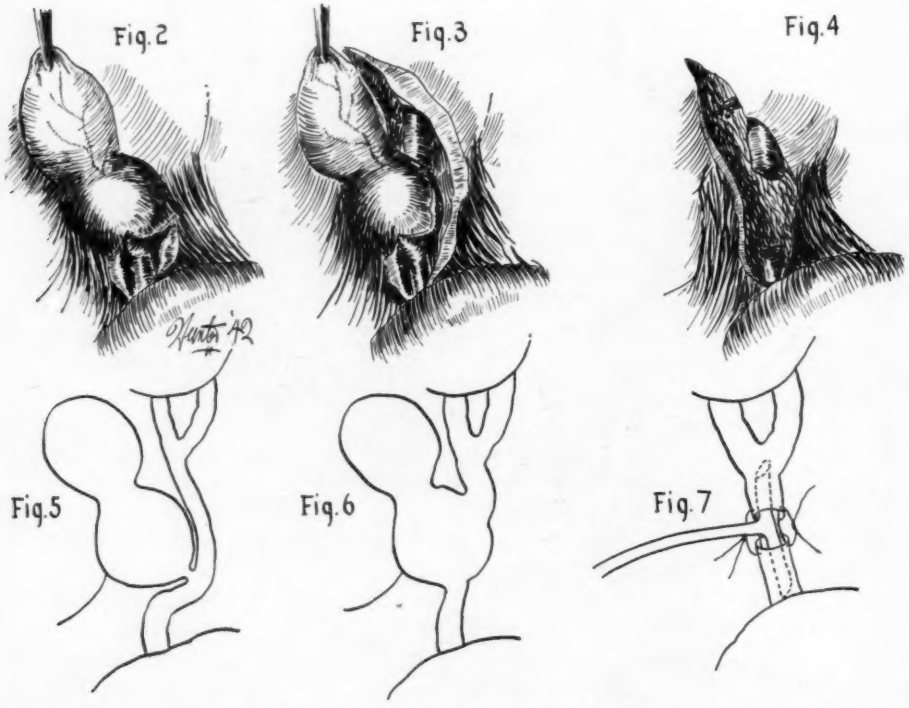

Fig. 2.—Shows duct leaving lower segment of gall bladder and passing down behind duodenum.

Fig. 3.—Shows second duct entering lower pouch of gall bladder from above.

Fig. 4.—Shows ends of divided ducts as seen after removing gall bladder.

Fig. 5.—Condition which had to be excluded, i.e., a short or absent cystic duct with the common duct closely adherent to the gall bladder.

Fig. 6.—Shows the arrangement actually present in this case.

Fig. 7.—Shows the duct ends being anastomosed over a T tube.

Discussion.—The unusual condition described presents many interesting points in connection with operative technique and possible etiology.

During the operation one's chief concern is to exclude the condition shown in Fig. 5, where with a very short cystic duct the neck of the gall bladder is densely adherent to the common duct. With the gall bladder opened and the orifices of the ducts visualized and demon-

strated by the passage of a probe into them, the true situation was clearly apparent. This demonstrates the value of opening the gall bladder during operation in certain puzzling cases.

The question of etiology of the condition reported is also of considerable interest. Several surgeons of extensive experience, with whom this case has been discussed, suggest that the condition was an acquired one.

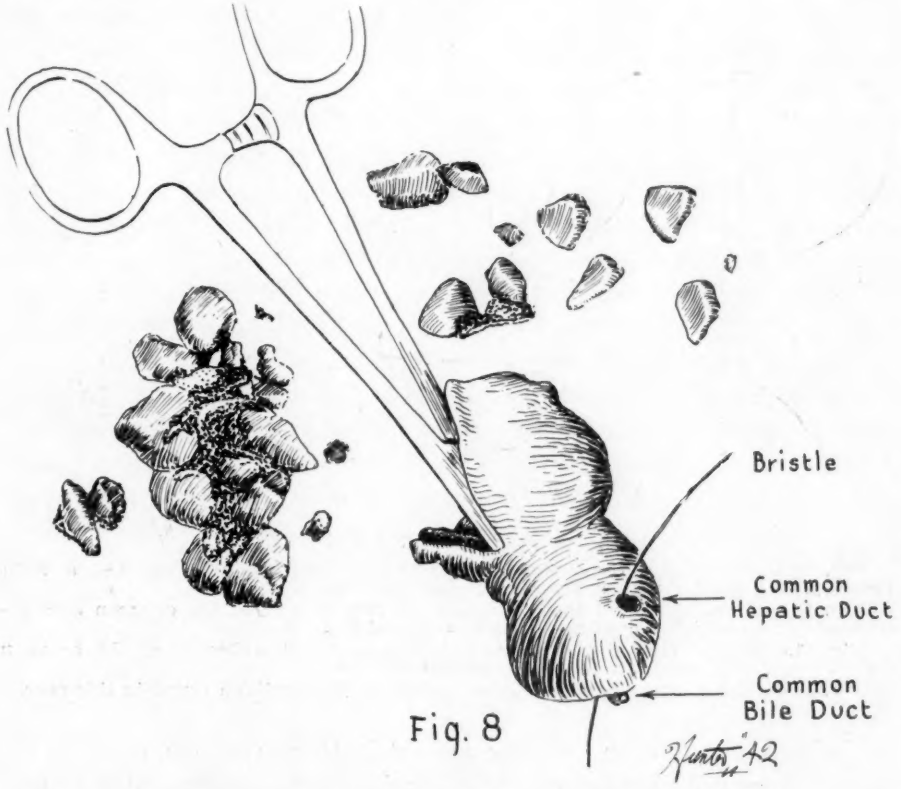

Fig. 8.—Shows specimen after removal with a bristle passing through the two duct openings and the tip of a forcep protruding through the lower or common duct opening.

In the presence of a short cystic duct, such as all surgeons have encountered at operation, it is possible that a stone in the duct might progressively enlarge causing a gradual dilation of the cystic duct as well as the adjacent common duct and neck of the gall bladder as shown in Fig. 12, *a* and *b*. The lower pouch of the "gall bladder" would then consist largely of dilated cystic duct. The fact that it lay entirely within the folds of the hepatoduodenal ligament lends color to this view as does the large mass of stones which was present.

The condition found in this case may also be explained on the basis of a congenital anomaly. One condition which must be considered is diverticulum of the common bile duct. Walton[1] has reported six per-

sonal cases and refers to between eighty and ninety similar cases reported by various authors. In his cases and those to which he referred, the gall bladder was present in its normal form and position but there was a large cystic pouch projecting from the lower portion of the common bile duct. This pouch was eccentric and projected to the right and extended above and behind the duodenum. The diverticulum resembled a saccular rather than a fusiform dilatation. This is

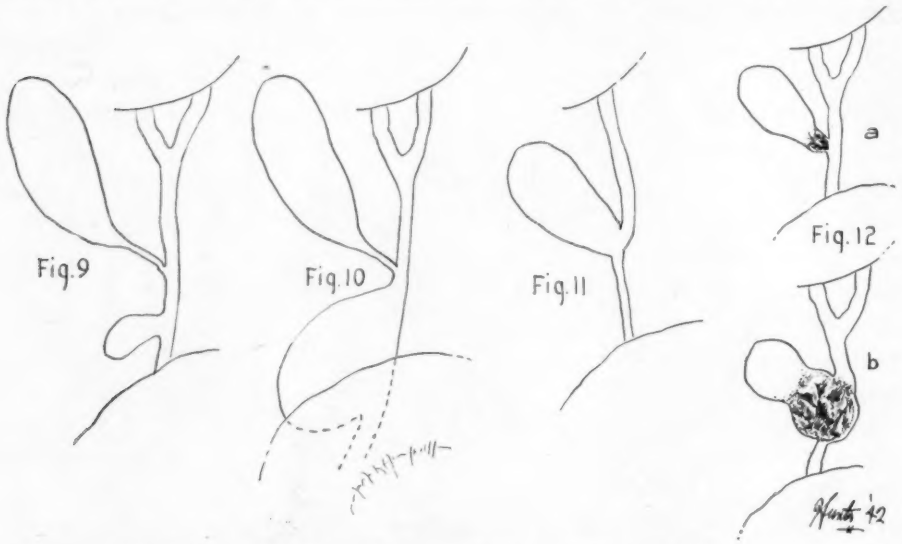

Fig. 9.—Illustrates a congenital anomaly as reported by Wolfson, i.e., a rudimentary gall bladder with a diverticulum of the common duct.

Fig. 10.—Shows the usual type of congenital diverticulum of the common duct associated with gall bladder of normal size and position.

Fig. 11.—Illustrates the type of anomaly caused by the absence of the common duct where the cystic duct enters the duodenum directly.

Fig. 12.—Illustrates a possible acquired origin of the condition found in this case.

probably the condition actually present in those cases reported in the literature as "Congenital Cystic Dilatation of the Common Bile Duct." Walton states that the opening of the common hepatic duct in the upper part of the sac was directly opposite that of the common bile duct below. They lay on the medial aspect of the pouch and were connected by a shallow groove. This suggested that only the lateral wall of the common duct was involved in the protrusion. He assumed that some congenital weakness existed in this part of the duct wall allowing it to protrude gradually as a saccular pouch (Fig. 10).

Wolfson[2] also reports a similar case in which there was a rudimentary gall bladder in the normal situation and a diverticulum of the common duct lower down containing calculi as shown in Fig. 9.

To make this explanation fit the case in point one would have to assume one of the two following conditions: (1) The occurrence of a diverticulum at the site of the cystic duct and represented in this case

by the lower pouch of the structure removed, the upper pouch being the true gall bladder; (2) the congenital absence of the normal gall bladder and the development of a diverticulum which represented the entire structure removed in this case.

Because the structure occupied the normal situation of the gall bladder and was attached to the under surface of the liver as usual, I am inclined to reject the explanation that it represents a congenital diverticulum.

The simplest and most logical explanation of the anomaly encountered in the case reported is an anomaly of the ducts, probably the congenital absence of the cystic duct. The hepatic duct entered the gall bladder from above and the common bile duct took exit from its lower aspect, the gall bladder forming the only connection between them. Walton[3] has reported a case of this type. Mentzner[4] points out that the cystic duct is very short in many cases and states that nine cases of true congenital absence of the cystic duct have been reported. All surgeons of experience have, of course, encountered the very short cystic duct at operation. Mentzner states further that in certain animals it is very short and is absent in the badger and baboon. He also makes the interesting statement that the anomalies found in man represent a reversion to the normal arrangement in certain animals. Mentzner also points out that the common duct is absent in some animals, the hepatic duct entering the gall bladder from above and the cystic duct entering the duodenum below. The cystic duct in these cases replaces the common duct (Fig. 11). Whether the duct connecting the gall bladder with the intestine is embryologically the cystic or the common duct, in the case recorded, one cannot say. Either anomaly, namely, the absence of the cystic duct or the absence of the common duct, would appear to adequately explain the condition found in this case. Of course, the large mass of stones found in the lower segment of the gall bladder representing Hartmann's pouch would cause distension of this segment with occlusion of the hepatic duct and production of the jaundice present in this case.

CONCLUSION

1. An unusual anomaly of the bile ducts is described and its possible etiology as a congenital or acquired condition is discussed.

2. The case presented considerable diagnostic interest because of the entire absence of pain in the presence of obstructive jaundice due to gallstones.

3. The technical difficulties are described and the following practical conclusions may be drawn:

(a) In every case of surgery upon the biliary tract thorough exposure of the hepatic, common, and cystic ducts is essential.

(b) If this is observed radical surgery may be safely carried out even in the presence of the most anomalous conditions.

(c) The value of opening the gall bladder in certain complicated cases for the purpose of exploration from within its cavity is emphasized.

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THE TREATMENT OF COMMON DUCT STONE MISSED AT OPERATION

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TO LEAVE a stone in the common or hepatic bile ducts during surgery on these structures is not a rare occurrence. Surgeons admit freely the high incidence of stones left in the biliary tree following surgery directed for their removal. The embarrassing facts associated with this situation are a continuance of the patient's symptoms of dyspepsia, pain, jaundice, chills and fever, and the high mortality rate associated with a secondary search for these stones. These secondary operations are so undesirable that any less difficult or hazardous procedure of dealing with the overlooked common duct stone is very acceptable.

The practice of using cholangiography at operation, as advocated by Mirizzi,[1] or postoperatively before removal of the T tube in the common bile duct,[2] has enabled the surgeon to determine quite accurately the presence or absence of obstruction to the outflow of bile from the biliary ducts.

By combining cholangiography and a study of varying pressure within the common bile duct under varying conditions, Walters and his associates made some very valuable findings on the physiology and pathologic physiology of the common bile duct,[3] together with the pharmacologic action of various drugs on this duct and the sphincter of Oddi.[4]

Pribram,[5] in 1935, reported the dissolution of stones in the common duct by the injection of ethyl ether through a drainage tube in the duct.

Walters and Wesson[6] report a case in which a common duct stone was caused to fragment by three daily injections of 5 c.c. of ethyl ether, and with two additional injections of one-third ethyl alcohol and two-thirds ether it passed into the duodenum with the aid of amyl nitrite inhalations as a relaxant to the sphincter of Oddi.

REPORT OF CASES

CASE 1.—Mrs. D., aged 33 years, entered the hospital, June 6, 1937, because of marked jaundice. Her present trouble began suddenly four weeks previously, with severe pain under the right costal arch, radiating into the subscapular area. Morphine administered hypodermically was required to control the pain, which lasted a few days and suddenly subsided. The temperature rose to 101° F. near the onset and gradually returned to normal. Definite jaundice was in evidence after two or three days and gradually increased to the time of admission.

The patient had a cesarean section five months previously. Her convalescence was complicated by thrombophlebitis and multiple pulmonary infarcts. A second incidence of thrombophlebitis caused her to remain in bed until about six weeks prior to this admission.

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Family history seemed irrelevant.

Examination.—The patient was obese, weighing 200 pounds. On admission the temperature was 98.4° F., pulse 84, and blood pressure 84/50. Skin and sclera were a deep yellow color. General physical examination was otherwise essentially negative. No definite tenderness, spasticity, or sense of mass could be made out in any part of the abdomen.

Bile graded 3+ was reported on urinalysis but only a faint trace was found in the stool. The urine, which had a specific gravity of 1.010, contained albumin 1+.

The white blood count was 5,800, the red blood count was 4,940,000, and the hemoglobin was 94 per cent.

The coagulation time was six minutes and the bleeding time was three minutes and forty-five seconds.*

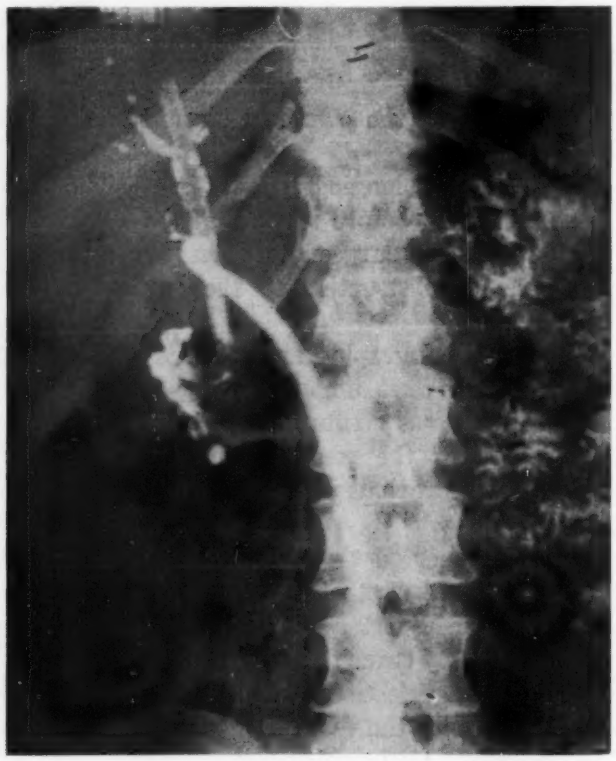

Fig. 14.—Postoperative cholangiogram of Case 1 showing shadow of stone in ampulla of Vater.

A diagnosis of obstructive jaundice was made and the patient prepared for surgery by intravenous solution of glucose, calcium gluconate, and small blood transfusions.

At operation, June 9, 1937, the common bile duct was found to be about 1 cm. in diameter. The common duct was opened and a probe passed easily into the duodenum and up either hepatic duct. The head of the pancreas seemed slightly enlarged. Prolonged exploration of the bile ducts failed to reveal evidence of obstruction. The liver was very dark in color and showed diffuse hepatitis grade 1+. The gall bladder was about normal size and showed moderate thickening. The gall bladder was removed and a T tube was placed in the common duct. The gall bladder showed mild chronic inflammatory changes and contained 3 to 4 c.c. of thick black bile.

*The prothrombin time was not in general use at this time.

Convalescence was quite satisfactory until the sixth postoperative day, when there was very free bleeding in the wound and around the drainage tube. Red blood count dropped to 1,440,000 and the hemoglobin to 37 per cent. Small daily transfusions were being given. After forty-eight hours the bleeding stopped temporarily and the red blood count and hemoglobin rose to 3,220,000 and 65 per cent respectively. On the fourteenth postoperative day there was further bleeding and the red blood count dropped to 2,760,000 and the hemoglobin to 53 per cent. At this time there had been very little bile from the T tube and little or no decrease in the jaundice. About the twentieth postoperative day the jaundice began to decrease, the bleeding ceased, and an increased amount of bile drained from the T tube. Special laboratory tests requiring vena puncture were omitted because of the inaccessibility of the veins and therefore the serum bilirubin levels were not known. Intravenous solutions and transfusions were given by continuous drip through a cannula tied in the vein. Subsequent progress was very satisfactory.

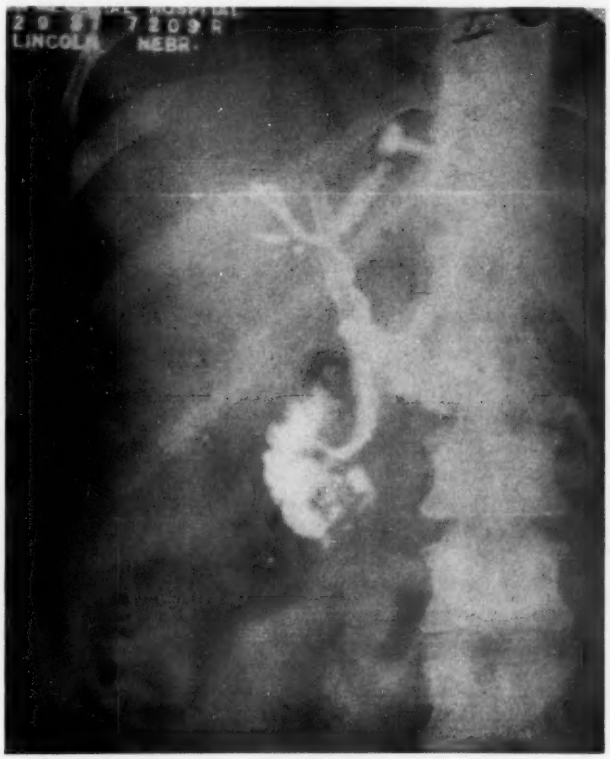

Fig. 1*B*.—Cholangiogram of Case 1 after dissolution of the common duct stone by the ether-alcohol mixture before removal of T tube.

On the thirty-fourth postoperative day a cholangiogram was made by injecting lipiodol through the T tube. A shadow interpreted as a stone was seen in the distal end of the common duct (Fig. 1*A*).

A mixture of one-third ethyl alcohol and two-thirds ethyl ether in amounts of 5 c.c. was injected daily into the T tube, for five days.

The following day a cholangiogram failed to show any evidence of stone (Fig. 1*B*). A subsequent cholangiographic study after three days revealed a prompt and free flow of the injected media into the duodenum. After the latter study the T tube was removed. The patient has remained well to date.

CASE 2.—Mrs. B., aged 37 years, entered the hospital, Aug. 19, 1941, because of severe right upper quadrant pain, jaundice, chills and fever. The present trouble began five days prior to admission, as a sudden, severe, sharp pain under the right costal arch, radiating to the tip of the right scapula. Two days later a yellow tint to the skin and sclera developed and gradually deepened. This was accompanied by chills and fever. Repeated hypodermic injections of morphine sulfate were required to control the pain.

In the past history was a story of a gall bladder type of dyspepsia of ten years' duration, with recurrent mild attacks of right upper quadrant distress.

The patient's father died at the age of 46 years from cancer of the colon. Family and personal history were otherwise essentially negative.

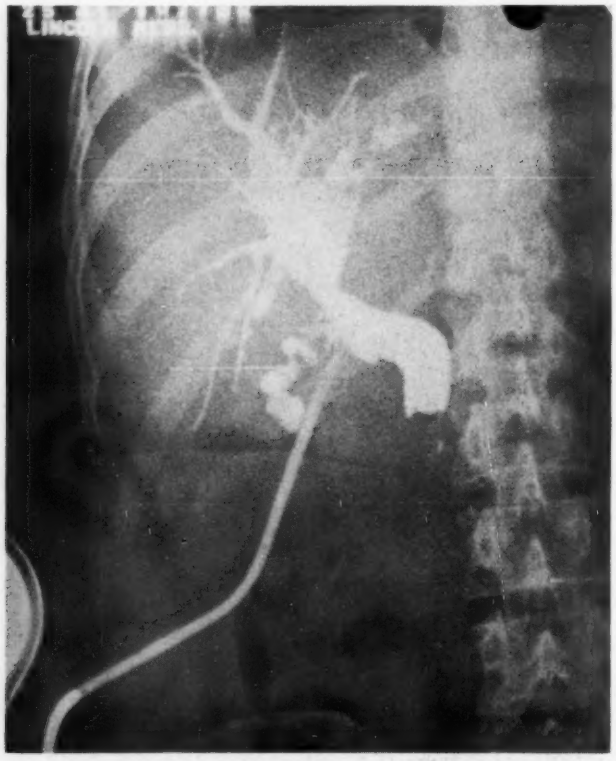

Fig. 2A.—Postoperative cholangiogram in Case 2 showing stone or stones impacted in the ampulla of Vater.

Examination revealed an obese female apparently very ill, with a temperature of 102° F., a pulse count of 142, and a blood pressure of 90/60. Other positive findings were a deep icteric tint of the skin and sclera, marked tachycardia, and moderate tenderness over the gall bladder, which was palpable below the costal margin.

Urinalysis of a catheterized urine specimen showed: Specific gravity 1.010; pH, 5.5; albumin, ++; bile, ++; pus and granular casts, +. The white blood count was 37,450 and the hemoglobin was 82 per cent. A Schilling hemogram showed a marked shift to the left. The prothrombin time was one minute and fifteen seconds (normal is twenty-three seconds). The van den Bergh test gave an immediate direct response with a value of 14.2 mg. per cent for serum bilirubin.

An electrocardiographic study was interpreted as showing a toxic myocardosis.

A diagnosis of acute cholecystitis and cholangitis was made. The high fever and leucocytosis were highly suggestive of a gangrenous condition of the gall bladder but the patient seemed desperately ill and in a state of mild shock, so that surgery was deferred and supportive measures instituted. Ten per cent glucose in saline solution with thiamin chloride was given intravenously in amounts of 3,000 c.c. in twenty-four hours. Sweetened fruit juices were offered per oram as tolerated.

An injection of 1 c.c. of synthetic vitamin K was administered intramuscularly. The patient was typed for transfusion and repeated white blood counts were ordered. The temperature rose rapidly to 105° F. and then receded. After eighteen hours the temperature and white blood count were markedly lower. Sulfathiazole therapy was instituted and after eight days the septic course had definitely subsided. Bile appeared in the stools at this time. The blood pressure was 120/80, pulse 96, and temperature 99 to 100° F. The white blood count was 15,000 and the prothrombin time was normal. A total period of twelve days was used for preoperative preparation. Intravenous fluids and glucose were gradually replaced by oral fluids, a high carbohydrate, high protein, low fat diet with supplemental high vitamin intake.

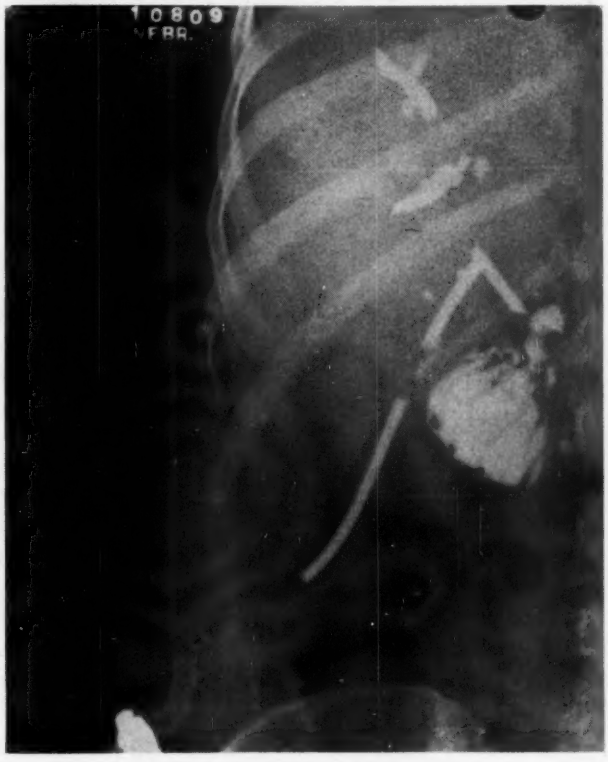

Fig. 2*B*.—Cholangiogram in Case 2 showing prompt passage of opaque media from common duct into the duodenum after the ether-alcohol injections.

At operation on the twelfth hospital day the gall bladder was found to be small, markedly thickened, and injected with a small gangrenous area at the fundus, which was adherent to the abdominal wall. It was filled with stones of various sizes. The great omentum was adherent to the gall bladder and bile ducts. The common bile duct was markedly dilated, surrounded by edematous tissue, and contained several large stones. The liver showed diffuse hepatitis grade 1.

The common duct was opened, the stones removed by scoop, and the common and hepatic ducts explored and flushed out with saline solution. The probes, scoops,

and irrigating solution passed freely and easily into the duodenum. A T tube was placed in the common duct. A subtotal cholecystectomy as advocated by Estes[7] was carried out and a tube inserted into the stump of the cystic duct.

In the first forty-eight-hour postoperative period the patient developed marked hyperpyrexia and an area of atelectasis in the lower lobe of the right lung posteriorly. The Trendelenburg position, carbon dioxide inhalations, and frequent change of posture were thought to contribute to a prompt disappearance of these complications. Bile began draining promptly and in good amount from both drainage tubes. The wound healed promptly and firmly.

An attempt to clamp the cystic duct and common duct tubes on the twelfth postoperative day produced epigastric distress, nausea and vomiting, and moderate fever. The tubes were permitted to drain and sulfathiazole was administered. Four days later this drug was discontinued because of a dermatitis.

Cholangiograms on the sixteenth and twenty-sixth days postoperatively revealed an obstruction in the common duct interpreted as a stone, or stones, in the ampulla of Vater (Fig. 2*A*).

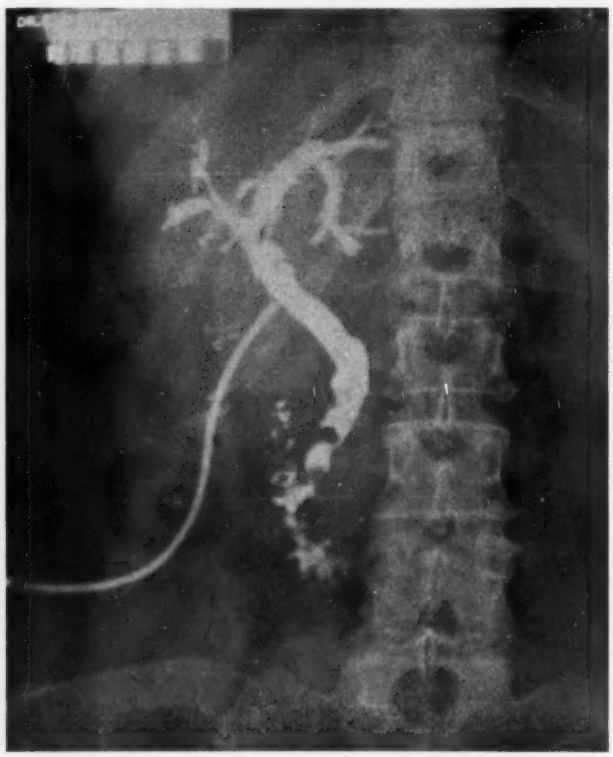

Fig. 3*A*.—A postoperative cholangiogram showing a filling defect which might be erroneously interpreted as a stone.

Six daily injections of a mixture of 4 c.c. of ether and 2 c.c. of ethyl alcohol into the T tube were given. After the fourth injection the stools, which had varied from clay color to light brown, became dark brown, and the epigastric distress disappeared. It was now possible to keep the T tube clamped constantly. The tube in the cystic duct had been removed and the second cholangiogram showed this tract to be closed. Cholangiograms on the day following the last instillation of the ether-alcohol mixture demonstrated a prompt and free discharge of the media from the common duct into the duodenum and failed to demonstrate any shadow of stone or other obstruction (Fig. 2*B*).

COMMENT

It has become common practice to explore and place some type of drainage tube in the common bile duct in cases of suspected or apparent stone or other obstructive pathology.

Employment of postoperative cholangiography permits the surgeon to evaluate the results of his operative efforts and discover any residual stone or other obstruction before the drain is removed. Attention should be called to the fact that a single cholangiogram may show obstruction which is the result of local spasm and be erroneously interpreted as organic obstruction. The value of taking a series of cholangiograms in one such case is shown in Figs. 3*A* and 3*B*.

Fig. 3*B*.—Cholangiogram of same case as Fig. 3*A*, taken a few minutes later and proving the fallacy of relying on a single cholangiogram.

The majority of gallstones show a high content of cholesterol, which dissolves or disintegrates readily by ether. This fact has been utilized to dissolve common duct stones missed at operation. This procedure has been successful in the cases here reported and is certainly preferable to a secondary operation.

Best and Hicken[8] have utilized the findings of other workers on the antispasmodic action of certain drugs on the sphincter of Oddi and the choleretic action of various substances together with bile duct irrigations in developing their "biliary flush." This is no doubt an excellent

procedure to overcome obstruction from spasm, inspissated bile, or very small stones but it does not seem feasible for the larger stones such as were demonstrated by the x-ray in the cases here reported. Best[9] has recently reported this limitation in the use of his nonoperative regime.

SUMMARY

Two cases of common bile duct calculus are reported in which stones remained in the duct after operation. In each case the stone was disintegrated by the action of ether and alcohol injected into the T tube. This dissolution of the stone and its passage into the duodenum were demonstrated by cholangiographic studies.

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THE EFFECT OF ANESTHETICS ON GASTRIC TONUS AND MOTILITY WITH SPECIAL REFERENCE TO ACUTE GASTRIC DILATATION*

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IT IS generally agreed that in acute dilatation of the stomach there is a loss of gastric muscle tonus with the result that accumulated secretions and gas can balloon out the relaxed viscus.[4, 6, 11, 12, 13, 15, 39] There is regurgitation of variable amounts of fluid. Dehydration, symptoms of toxemia, and collapse are features of the condition if it is progressive and unrelieved.

It seems clear from the work of Dragstedt and others[13] that, once the stomach has become dilated, the main factor in the pathogenesis of the condition is the failure of the gastric and pancreatic juices to be reabsorbed. These secretions stagnate in the atonic stomach or are lost by regurgitation, and fail to reach the lower absorbing portion of the gastrointestinal tract. Water and the inorganic elements, sodium and chloride, are lost from the blood plasma. Dehydration and alkalosis result and, unless the fluid and electrolytic balance is re-established, death results.

The problem then seems to be: Why does the stomach become atonic in the first place and in some cases remain so for a considerable length of time, even in spite of treatment? Clinically, acute gastric dilatation has been observed in association with a wide variety of conditions, among which may be mentioned its occurrence following an attack of migraine,[20] during the course of pulmonary tuberculosis,[34] in severe diabetes,[1] and following various operative procedures.[13] There are, undoubtedly, multiple etiologic factors. In the majority of cases, however, the condition has occurred postoperatively, and in these cases it has occurred most frequently following laparotomy among patients who have had a general anesthetic. It has been only natural to look to the effects on the stomach incident to operation, either the operative procedure itself or the anesthetic or both, in seeking an explanation of this complication.

Dragstedt[12] reviewed the question of the causation of acute postoperative gastric dilatation and concluded that the primary cause for the reduction of gastric tonus is an inhibition caused by reflex stimulation of vagus and splanchnic nerves to the stomach during the course of the operation. This author noted, however, that no amount of stimulation

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of these nerves in the experimental animal would produce the condition and he concluded that, in addition, the gastric musculature must be depressed by the anesthetic in order for the symptom complex to be produced. It is with the role of anesthesia as a possible etiologic factor that the present investigation is concerned.

Kelling found that he could produce an enormous degree of gastric distention in dogs by pumping in air through a gastrostomy opening if the animals were first anesthetized. In unanesthetized dogs he could produce only a moderate degree of distention because regurgitation through the esophagus emptied the stomach as soon as the intragastric pressure rose.

Báron and Bársony carried out roentgenoscopic studies on the gastrointestinal tract of dogs during anesthesia with chloroform and ether. They observed marked relaxation of the stomach with both these agents. Peristalsis was abolished. In some cases full relaxation persisted for one hour after discontinuance of the anesthetic and recovery was complete only after three or four hours.

Miller, using the balloon-recording method, studied the effects of general anesthesia on the muscular activity of the gastrointestinal tract of dogs that had permanent fistulas. This investigator observed a decrease in gastric tonus and a reduction in motility during third stage anesthesia with ether and chloroform. In some instances the stomach was still somewhat depressed as long as five hours after recovery of consciousness. With nitrous oxide, after administration of the anesthetic had been discontinued, there were a decrease of tonus and a reduction in motility similar to those which occurred with ether anesthesia.

Bisgard and Johnson found gastric tonus and motility to be depressed by ether and nitrous oxide in both man and dog. On the other hand, these workers found that with some agents, notably cyclopropane-oxygen alone, and especially cyclopropane-oxygen as a supplement to a basal anesthetic of avertin with amylene hydrate, gastric activity was increased. They suggested that this difference in action might be dependent on the relative quantity of oxygen in the blood and tissues during anesthesia. Another explanation which has been offered concerning the difference in action observed with different anesthetics is that the effects of some agents might be mediated through the sympathetic nervous system and other agents might affect the gastric musculature directly.[7]

The effect of anesthesia on gastric tonus and motility is of further interest in view of the ever-increasing use of newer and special anesthetic agents which are employed alone or in combination with other agents. The trend toward the more frequent use of the newer agents may be seen from the periodic clinical reports on anesthesia such as those of Lundy and his associates.[23]

In order to evaluate more properly the question of anesthesia as a possible etiologic factor in acute gastric dilatation, it was decided to make a comparative study of the effects of anesthetics, including some

of the newer agents and combinations of agents, on the gastric tonus and motility of the dog under the following conditions: (1) in animals in which the extrinsic gastric nerves were present; (2) after bilateral splanchnicectomy and double vagotomy; (3) after bilateral splanchnicectomy only; and (4) after double vagotomy only.

METHOD

The effects of anesthetics on the motor activity of the stomach were studied in dogs that had permanent gastric fistulas. Young healthy dogs weighing 7 to 16 kg. were selected and trained to lie quietly on the right side. The Mann-Bollman type of fistula was employed (Fig. 1). This was prepared by a two-stage procedure. In the first stage a loop

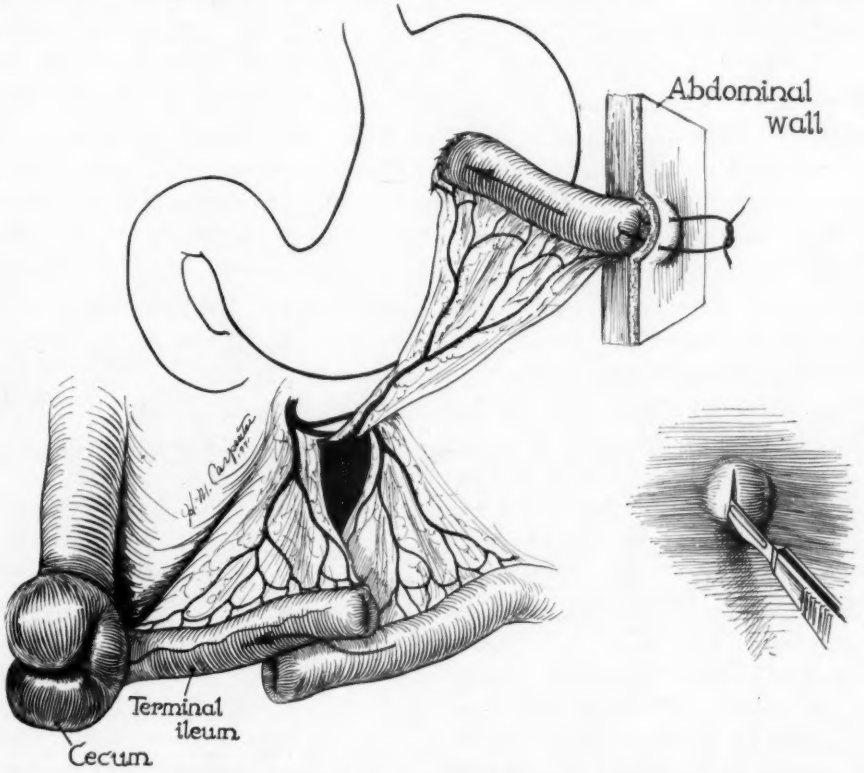

Fig. 1.—Mann-Bollman fistula; distal (aboral) end of isolated loop of terminal ileum anastomosed to stomach, proximal (oral) end closed and anchored in subcutaneous position; continuity of ileum established; direction of peristaltic activity indicated by arrows; closed loop of ileum converted into a fistula by opening it through a short skin incision.

of the terminal portion of the ileum 8 to 10 cm. in length was isolated. The continuity of the ileum was established by a side-to-side anastomosis. The distal (aboral) end of the loop was anastomosed to the stomach near the middle of the corpus; the proximal (oral) end was closed, passed through a stab wound in the upper portion of the left rectus muscle, and anchored in a subcutaneous position. The abdomen was closed in layers. The proximal end of the loop was closed and left beneath the

skin to protect the gastroenteric anastomosis from bacterial contamination from the skin surface. Two weeks after the first procedure the closed loop of ileum was converted into a fistula by opening it through a short incision in the skin and suturing the edges to the margin of the skin. By giving the loop this relation with respect to the stomach and the abdominal wall, peristaltic activity is directed toward the former and away from the latter. In no instance was there leakage of gastric contents on the skin of the abdominal wall. The dogs appeared perfectly normal after establishment of these fistulas, and the latter were still functioning well at the time of necropsy, which was in some instances as long as thirteen months after the fistulas had been established.

The apparatus used to record the motor activity of the stomach was the balloon-bromoform manometer apparatus similar to that described by Carlson. A deflated condom balloon attached to the end of a No. 20 French hard rubber catheter was passed through the fistula into the stomach. The other end of the catheter was attached to a rubber tube connected with the manometer. One hundred and eighty cubic centimeters of air were introduced into the balloon; this amounted to a pressure of 2 to 6 cm. bromoform. The volume was not sufficient to stretch the walls of the balloon. A writing lever attached to a float riding on the column of bromoform recorded the activity of the stomach on a slowly revolving kymograph. Because this method records changes of diaphragmatic pressure, a concomitant record of the respiratory excursions was made by a standard pneumographic method.

The tracings obtained by this technique show contractions and alterations in tone of the gastric musculature. The latter are represented by changes in the level of the "diastolic" line of the tracing.

The animals were fasted for eighteen to twenty-four hours preceding each experiment. A control observation of fifteen to thirty minutes was made before each anesthetic was given. The most frequently observed type of contractions during the control period was type II, according to the criteria of Carlson. In this type of contractions the tonus of the stomach is relatively high and the contractions follow one another in rapid succession. The duration of the contractions varies between twenty and thirty seconds. The contractions may vary to some extent in amplitude and rate, but otherwise are practically continuous.

Observations were not made during the periods of induction of, nor reactions from, the anesthetics because during these periods exaggerated respiratory excursions and bodily movements made recording of gastric motor activity impossible. Observations were made at various intervals after administration of the anesthetics had been discontinued until gastric tonus and motility had returned to the control level.

The anesthetic gases were administered by means of an apparatus which allows rebreathing of the gases and which was designed by Mousel and Seldon for use on laboratory animals. Carbon dioxide was absorbed from the exhaled gases by means of soda lime. This apparatus was attached to a standard clinical gas machine.

An attempt was made to determine the position of the balloon in the stomach roentgenographically. This was not entirely satisfactory. In order to outline the walls of the stomach accurately in relation to the balloon it was necessary to introduce a considerable amount of contrast medium into the stomach. This represented the position of the balloon in a partially filled stomach and did not meet the conditions of this investigation. Accordingly, when all experiments were completed, laparotomy was performed on three fasted dogs and the position of the balloon was determined by inspection, after which the dogs were killed. Laparotomy was performed under pentothal sodium anesthesia. In all instances the stomach was found contracted on the balloon which occupied the proximal portion of the prepyloric region, all of the corpus, and most of the fundus, as was determined by palpation and verified by direct inspection after the stomach had been opened.

Observations of the effects of anesthetics on gastric tonus and motility were repeated after splanchnicectomy and vagotomy. For this denervation a two-stage procedure was employed. The first stage consisted of a thoracic approach through the eighth interspace on the left side. Segments measuring 2 cm. in length were removed from each of the vagal trunks as they lie on either side of the esophagus immediately above the esophageal hiatus of the diaphragm. In this location the trunks have been formed from the pulmonary plexus but have not yet divided into the various rami which supply the stomach and other abdominal viscera. The lower seven sympathetic ganglia and connecting chain, as well as the emergent splanchnic nerves in practically their entire extent, were removed. When recovery was complete, usually after two to three weeks, splanchnicectomy was performed through the eighth interspace on the right side in a manner identical with that employed on the left. Bilateral splanchnicectomy and double vagotomy were performed on four dogs by this two-stage procedure.

Transthoracic double vagotomy only was done on two dogs and bilateral splanchnicectomy only was performed on two dogs by the procedures herein described. All dogs on which double vagotomy was performed vomited for a few days after the operation. This occurred shortly after feeding but not all the food ingested was lost by vomiting. Ultimately the vomiting ceased altogether and the dogs appeared perfectly normal. There was no vomiting in the dogs submitted to bilateral splanchnicectomy only.

RESULTS

A. Effects of Anesthetics on Gastric Tonus and Motility in Animals in Which the Extrinsic Gastric Nerves Are Intact.

1. *Ether* (Fig. 2*a*).—The effect of ether anesthesia on gastric tonus and motility was studied in twelve dogs. Induction of anesthesia was carried out by the open drop method. Anesthesia was carried to plane

2 of the third stage, according to the criteria of Guedel, and maintained as nearly as possible at the level for fifteen minutes. In every instance gastric tonus was greatly diminished and motility completely abolished. The time required for tonus and motility to return to normal was from one hour and fifteen minutes to ten hours. In eight dogs the motor activity had returned to normal two to three hours after the anesthetic was discontinued. Usually tonus began to return before motility; otherwise tonus and motility returned together.

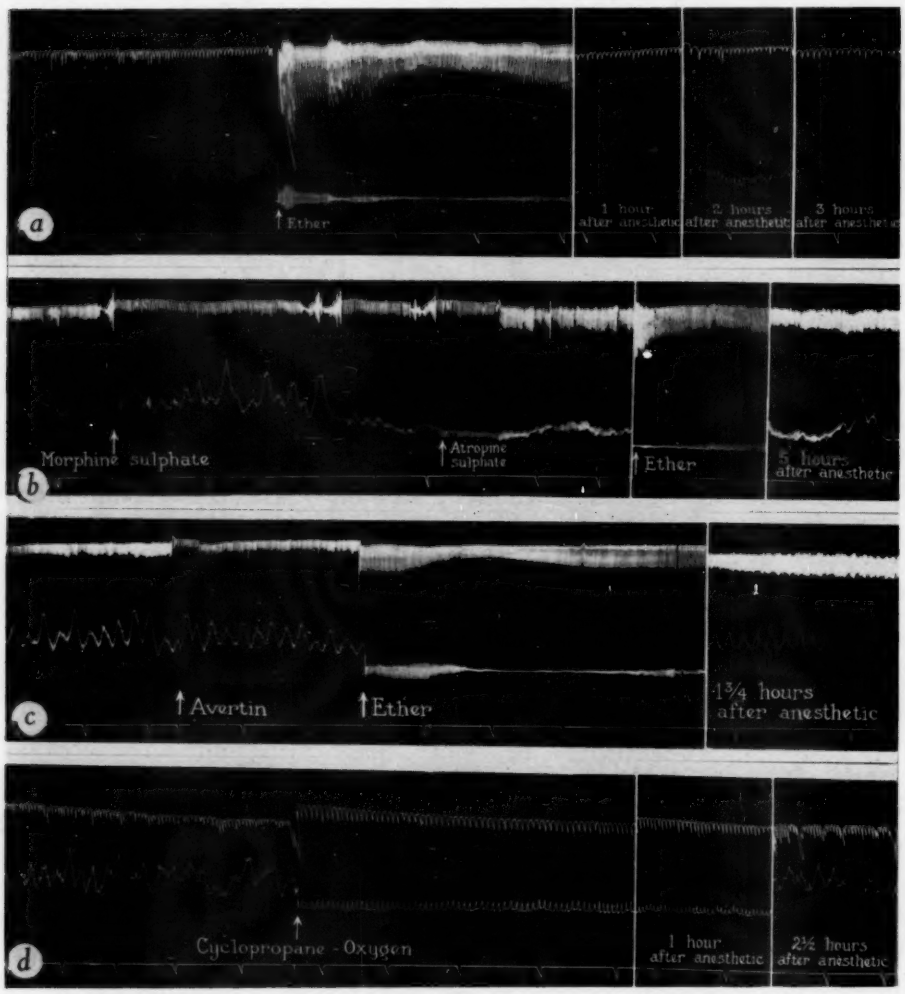

Fig. 2.—Effect of anesthesia on gastric contractions. *a*, Ether anesthesia, Dog 11 (weight 11 kg.). Upper tracing in this and subsequent figures shows respiratory excursions; middle tracing shows gastric contractions and superimposed diaphragmatic pressure changes; third stage anesthesia indicated by arrow; time interval in this and subsequent figures one minute.

b, Ether anesthesia with premedication of morphine and atropine, Dog 7 (weight 15.5 kg.). Morphine sulfate, 7.75 mg., and atropine sulfate, 0.3 mg., given hypodermically; third stage ether anesthesia indicated by arrow.

c, Ether supplemental to a basal anesthetic of avertin, Dog 11 (weight 11 kg.). First arrow thirty minutes after avertin in amylene hydrate, 1.1 c.c. in 44 c.c. water, given by rectum; third stage anesthesia indicated by second arrow.

d, Cyclopropane-oxygen anesthesia, Dog 4 (weight 9 kg.). Third stage anesthesia indicated by arrow.

2. *Ether With Premedication of Morphine and Atropine* (Fig. 2*b*).—Observations were made on six dogs. Morphine sulfate in doses of 0.5 to 0.75 mg. per kilogram of body weight and atropine sulfate in a dose of 0.023 mg. per kilogram of body weight were given hypodermically. Morphine in this dosage produced a state of drowsiness in the dog which was thought comparable to that produced in man after the usual preoperative administration of morphine.

In all observations after the administration of morphine there was a transient increase in gastric tonus and motility followed by a marked decrease in motility and a moderate reduction in tonus. There was little further effect on gastric activity after the administration of atropine. After etherization to the third stage there were a further decrease in tonus and complete loss of motility. The average time required for tonus and motility to return to normal was five hours and fifteen minutes.

3. *Nitrous Oxide-Oxygen and Ether.*—Observations were made on six dogs. For these experiments an ether vaporizer was attached to the gas machine. With nitrous oxide-oxygen the animals were anesthetized as deeply as possible without producing cyanosis. Ether was then added and the degree of anesthesia was carried as nearly as possible to plane 2 of the third stage and held there for fifteen minutes. Very little skeletal muscular relaxation was produced by the gas-oxygen alone and during this period gastric motor activity was unaffected. After ether was added and anesthesia carried to the third stage, there was marked reduction in gastric tonus and motility was entirely abolished. The time required for tonus and motility to return to normal fell within the range of that required for ether alone.

4. *Ether Supplemental to a Basal Anesthetic of Avertin With Amylene Hydrate* (Fig. 2*c*).—Observations were made on five dogs. Avertin with amylene hydrate in a dose of 100 mg. per kilogram of body weight was administered thirty minutes before ether was given. With avertin, gastric motor activity was unaffected in three dogs. In two dogs the amplitude of contractions was moderately reduced. In all instances, after anesthesia was carried to the third stage with ether, the effect on gastric tonus and motility was the same as with ether alone.

5. *Prolonged Ether Anesthesia.*—The effect of prolonging ether anesthesia on gastric motor activity was studied in five dogs. Third stage ether anesthesia was maintained for one hour and fifteen minutes. The results were very similar to those obtained with the fifteen-minute period of ether anesthesia. The time required for tonus and motility to return to normal averaged ten minutes longer than that required when ether anesthesia was maintained for only fifteen minutes.

6. *Cyclopropane-Oxygen* (Fig. 2*d*).—The effect of cyclopropane-oxygen anesthesia on gastric motor activity was studied in seven dogs. Anesthesia was carried to plane 2 of the third stage and maintained at the level for fifteen minutes. Skeletal muscular relaxation was thought to

be as complete as that observed with ether. The effect on gastric motor activity was strikingly similar to that of ether. Gastric tonus was greatly diminished and motility entirely abolished. The average time required for motor activity to return to normal in all observations was two hours and forty-five minutes.

7. *Cyclopropane-Oxygen Supplemental to a Basal Anesthetic of Avertin With Amylene Hydrate.*—Observations were made on four dogs. The effect of cyclopropane-oxygen on gastric tonus and motility was not altered when these agents were supplemental to a basal anesthetic of

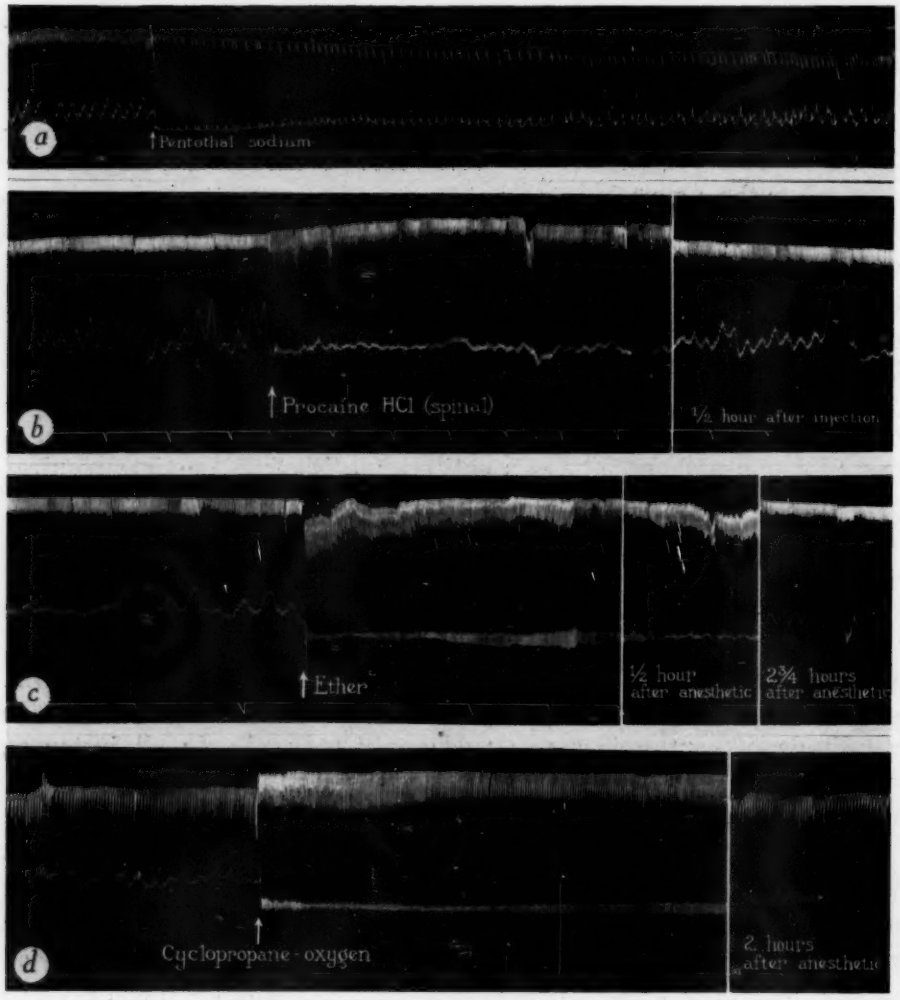

Fig. 3.—Effect of anesthesia on gastric contractions. *a*, Pentothal sodium anesthesia, Dog 5 (weight 12.5 kg.). Pentothal sodium 0.3 Gm. in 5 per cent aqueous solution given intravenously.

b, Spinal anesthesia, Dog 7 (weight 15.5 kg.). Procaine hydrochloride, 75 mg. in 3 c.c. physiologic salt solution injected in subarachnoid space between spines of last thoracic and first lumbar vertebrae; sensory loss demonstrated at upper thoracic level.

c, Ether anesthesia after bilateral splanchnicectomy and double vagotomy, Dog 6 (weight 12 kg.); third stage anesthesia indicated by arrow.

d, Cyclopropane-oxygen anesthesia after bilateral splanchnicectomy and double vagotomy, Dog 8 (weight 11 kg.); third stage anesthesia indicated by arrow.

avertin with amylene hydrate in a dose of 100 mg. per kilogram of body weight.

8. *Nitrous Oxide-Oxygen.*—Observations were made on eight dogs. Anesthesia carried as deeply as possible with nitrous oxide-oxygen without producing cyanosis did not affect gastric tonus or motility. In these instances there was very little skeletal muscular relaxation.

A depth of anesthesia sufficient to produce skeletal muscular relaxation was always accompanied by cyanosis. In these observations the effects on gastric tonus and motility were very similar to those obtained with ether.

9. *Ethylene-Oxygen.*—The effect of ethylene-oxygen on gastric motor activity was studied in seven dogs. In four dogs, third stage anesthesia with moderate skeletal muscular relaxation was produced, unaccompanied by cyanosis. There were a moderate decrease in tonus and a complete abolition of motility in these instances. The average time required for tonus and motility to return to normal was one hour.

In three dogs a depth of anesthesia sufficient to cause skeletal muscular relaxation could not be obtained without producing cyanosis. In these observations there was little effect on gastric tonus and motility.

10. *Intravenous Pentothal Sodium* (Fig. 3*a*).—Observations were made on seven dogs. Pentothal sodium in a 5 per cent aqueous solution was administered intravenously. Anesthesia was carried to the third stage according to the criteria of Lundy.[22] Twenty-three to twenty-eight milligrams of pentothal sodium per kilogram of body weight were required.

In five dogs there were a transient reduction in tonus and a decrease in motility immediately after injection of the drug. In all of these observations tonus and motility had returned to normal before the animal was awake. In two dogs gastric tonus and motility were unaffected by third stage anesthesia produced by the intravenous injection of pentothal sodium.

11. *Intravenous Administration of Pentothal Sodium Supplemented With Nitrous Oxide-Oxygen.*—The effect on gastric motor activity of intravenous administration of pentothal sodium supplemented with nitrous oxide-oxygen was studied in seven dogs. Pentothal sodium in doses of 15 to 20 mg. per kilogram of body weight was given intravenously and the animals were allowed to breathe a gas mixture composed of equal parts of nitrous oxide and oxygen. In all observations there was no effect on gastric tonus or motility.

12. *Spinal Anesthesia* (Fig. 3*b*).—Observations were made on seven dogs. To facilitate lumbar puncture the dogs were placed on the Delahanty table as modified by Essex and Lundy. A 2.5 per cent solution of procaine hydrochloride in doses of 3.3 to 6.8 mg. per kilogram of body weight was used. Injection of anesthetic solution was done between the spines of the last thoracic and first lumbar, or between those of the first

and second lumbar vertebrae. The criteria used to determine a successful experiment were the free aspiration of spinal fluid before and after the injection, complete paralysis of the hind legs, and the demonstration of a sensory loss at the upper thoracic level.

In four dogs there was a diminution of the amplitude of gastric contractions with no reduction in tonus. In three dogs, in addition to a diminution in the amplitude of contractions there was a moderate reduction in tonus. Gastric tonus and motility returned to normal about the time the first movements of the hind legs were noted.

B. Effects of Anesthetics on Gastric Tonus and Motility After Splanchnicectomy and Vagotomy.

The effect of the anesthetics used in the innervated group of animals was studied in four dogs on which bilateral splanchnicectomy and double vagotomy had been performed, in two dogs on which bilateral splanchnicectomy only had been performed, and in two dogs on which double vagotomy only had been performed. In all three of these groups of denervated animals the effect of anesthetics on gastric tonus and motility was essentially the same as observed in the innervated group of animals (representative tracings, Fig. 3*c* and *d*).

COMMENT

It can be seen that anesthetics had either a depressing effect on gastric tonus and motility or no effect at all. The decrease in activity was, in a general way, directly proportional to the degree of anesthesia produced, regardless of the agent used. Anesthesia carried to plane 2 of the third stage by any of the inhalation anesthetics, whether employed alone, in combination with another inhalation anesthetic, or supplemental to a basal anesthetic of avertin with amylene hydrate, caused a marked reduction in gastric tonus and complete cessation of motility. Since the effect of these anesthetics in the three groups of denervated animals was essentially the same as in the innervated group, it was concluded that the effect was primarily on the peripheral gastric motor mechanism and was not mediated through the splanchnic or vagus nerves.

It is believed that the reduction in gastric tonus was not an expression of decreased intra-abdominal pressure caused by loss of tone of the abdominal musculature. In many experiments, gastric tonus did not return to normal for as long as several hours after the animal had completely regained use of the skeletal muscles.

The question may be asked whether the experiments done after denervation were carried out before the vagus and splanchnic nerves had regenerated. The recent observations of Hinsey and associates and those of Hollinshead and Finkelstein have served to emphasize the importance of functional control of regeneration in work on sympathectomized animals. When all the experiments in the present investigation were finished, the dogs on which denervation had been performed were killed

by bleeding under pentothal sodium anesthesia and at necropsy an attempt was made to determine whether the splanchnic or vagus nerves had regenerated. It was found that the vagi had not regenerated. This is in accord with the work of Vanzant who, using the same technique for double vagotomy that was employed in this study, showed that there was no regeneration of the vagus nerves of the dog when examined two to three years after vagotomy. In one dog on which necropsy was performed eleven weeks after splanchnicectomy, no tissue replacement could be found between the severed ends of the nerves. In the remaining five dogs on which splanchnicectomy had been done, some fairly well-defined strands of replacement tissue were found at the site of the original denervation. Necropsy was performed on these five dogs longer than five months after splanchnicectomy. In two dogs this tissue replacement was carefully resected and prepared for microscopic study. Nerve tissue was found in the entire course of the site of the original operation. Necropsy was performed on these two dogs eight months after splanchnicectomy. This observation undoubtedly represented regeneration of these nerves. Most of the experiments carried out after splanchnicectomy were done within a period of eight weeks after denervation and many were done as soon as four and one-half weeks after denervation. It is believed that very little, if any, regeneration of these nerves had taken place by that time, especially in view of the fact that very extensive splanchnicectomy was performed.

There was very little evidence to indicate that the decrease in gastric tonus and motility was dependent on the relative quantity of oxygen in the blood and tissues during anesthesia. It is true that with nitrous oxide-oxygen, in order to anesthetize the dog deeply enough to permit satisfactory observation, it was necessary to increase the concentration of nitrous oxide to the point of cyanosis. Just what effects were due to anoxia and what effects were due to the concentration of nitrous oxide in the blood is impossible to say. Cyclopropane-oxygen anesthesia depressed gastric motor activity much more than did ethylene-oxygen anesthesia, even when some cyanosis was produced with the latter agent.

Apparently the depth is more important than the duration of anesthesia in relation to the effects on gastric tonus and motility. Increasing the duration of ether anesthesia fivefold prolonged the depressing effect very little. This is in agreement with the work of Cannon and Murphy[8] on cats. These workers measured the gastric emptying time by means of the roentgenoscopic method after etherization. They found that anesthesia maintained for one-half hour prolonged gastric emptying very nearly as long as when anesthesia was maintained triple that time.

A rather striking individual susceptibility to the depressing effect on gastric tonus and motility was exhibited by the dogs in this investigation. In some dogs there was a tendency for a quicker return of motor activity no matter what anesthetic was employed; in others a relatively greater

time elapsed before tonus and motility returned to normal after discontinuance of the anesthetic. This difference of reaction to anesthesia did not seem to be dependent on the nutritional state, emotional make-up, age or weight of the animal, nor on the type of gastric contractions observed during the preanesthetic control period.

We have no explanation for the decrease in gastric motor activity which was observed during spinal anesthesia. Before this work was undertaken, it was thought that this method would cause an increase in activity similar to its reported effect on the small intestine. The explanation given for the increase in activity in the small bowel during spinal anesthesia is that the inhibitory influence mediated through the splanchnic nerves is abolished by blocking conduction through these nerves with procaine.[3, 26, 29] After observing a decrease in gastric activity during the course of the first few experiments, we felt that the spinal anesthesia was not sufficiently high to involve the splanchnic supply to the stomach. This idea was given weight by the work of Barron, Curtis, and Lauer. These workers observed a decrease in gastric tonus and motility with the balloon-recording method in patients during herniorrhaphy under spinal anesthesia. They did not observe any evidence of splanchnic paralysis and concluded that the gastric paresis was due to reflex stimulation of the splanchnic nerves during the course of the operation.

Accordingly, experiments were continued in which progressively greater amounts of procaine were employed until a definite sensory loss was demonstrated in the region of the upper thoracic level and in a few instances at the lower cervical level. This proved to make no difference in the effects on gastric tonus and motility; activity was depressed in all experiments. The excitement which may attend the performance of spinal anesthesia in some instances was ruled out as a possible cause for these results early in the course of the experiments when the technique of spinal anesthesia on the dog was being learned. Many unsuccessful attempts to insert the needle into the subarachnoid space did not affect gastric activity.

The fact that the same decrease in gastric activity during spinal anesthesia was observed after splanchnicectomy led to a consideration of some other mechanism not dependent on the presence of the splanchnic nerves to account for this effect. The possibility that procaine circulating through the blood stream might affect the peripheral gastric motor mechanism directly was considered but the injection of large amounts of procaine in the region of the spinal cord, but not in the subarachnoid space, failed to decrease gastric tonus and motility. What effect a lowering of the blood pressure due to spinal anesthesia would have is not known. There is the possibility that the decrease in gastric activity might be dependent on the effect of spinal anesthesia on the small bowel. It has been shown, for instance, that handling of the small bowel causes a decrease of gastric motor activity whether the splanchnic nerves are intact or not.[9]

Premedication with morphine and atropine definitely prolonged the depressing effect of ether. From a review of some of the experimental work relative to the action of morphine and atropine on gastric motor activity, no general conclusion concerning the action of morphine on gastric tonus and motility can be made, although it is generally conceded that atropine causes a decrease in activity.[5, 18, 24, 32, 33, 35, 36, 38] This is in part understandable when consideration is given to the method of investigation and the species of animal investigated. When the action of morphine was studied in the dog by means of the balloon-recording method,[5, 32] the results were fairly consistent. There was a marked decrease in activity lasting for several hours. In the light of these observations it would appear that the prolongation of the depressing effect of ether on gastric tonus and motility after premedication with morphine and atropine which was observed in the present study could be explained.

When the action of morphine on man was studied, most of the available evidence showed that the action of morphine on the walls of the stomach was predominantly motor.[5, 35, 36, 38] There is undoubtedly a species difference. Veach, on the basis of his results in human subjects, recommended the use of morphine in the treatment of acute dilatation of the stomach. In view of the work of Schapiro and that of Van den Velden, which showed that gastric emptying in man may be considerably prolonged by morphine, presumably by tonic contraction of the pylorus, the rationale of the use of morphine in the treatment of acute gastric dilatation is open to question.

If the same situation obtains in man as was found in the dog, it may be seen that considerable gastric atony may follow deep general anesthesia, presumably by a direct effect on the peripheral gastric motor mechanism. This should take on more significance if it is true that the human gastric motor mechanism is depressed more by anesthesia than that of the dog[31] and if the same individual susceptibility to anesthesia prevails in man as was observed in the dog. It may be that, if block anesthesia of peripheral nerves were employed in conjunction with a lesser degree of general anesthesia, there would be less postoperative gastric atony attributable to the anesthetic agents.

Dragstedt's[12] contention that the loss of gastric tonus in acute postoperative gastric dilatation is a result of the effect of operative trauma plus the effect of anesthesia may be true. It is reasonable to suppose that each of these factors would take on relatively greater or less significance in a given case, depending on the degree of anesthesia and the nature and extent of the operative trauma. In this connection the work of Cannon and Murphy[8] is of interest. These investigators, in studying the conditions attending operation as possible causes of postoperative paralysis of the alimentary canal, measured the degree of discharge of food from the stomach of the cat by the roentgenoscopic method. They found that etherization caused some delay in emptying. Etherization plus laparotomy, exposure of the gut to the air, and minimal cooling

caused no more delay in gastric emptying than did ether alone. By far the most striking effects were seen after handling of the digestive organs. Even with the most gentle handling within the peritoneal cavity or under warm salt solution no gastric peristalsis was seen and no food left the stomach for hours.

If comparatively little gastric atony were found to develop postoperatively among patients who had had pentothal sodium, nitrous oxide-oxygen alone, or ethylene-oxygen alone, it might be argued, on the basis of the results of this investigation, that this was because these agents do not depress gastric motor activity to any great extent. While this might be true in part, it does not tell the whole story. By virtue of the scope of operation permitted under these agents, the operative trauma is different from the trauma in those procedures requiring complete muscular relaxation. Certainly the extent of trauma would be less in most cases. More experimental work is definitely needed to clarify the effects that various operative procedures per se have on gastric motor activity.

There is probably some gastric atony after every operative procedure but the occurrence of the more advanced stages of acute dilatation of the stomach appears to be infrequent at the present time. Aside from any change in the etiologic factors in acute gastric dilatation, the lessened incidence of the condition would seem to be due in a large measure to better postoperative care. The aspiration of the collected fluid and gas from the stomach and more general application of the principle of continuous gastric aspiration as advocated by Paine and Wangensteen, together with the replacement of lost fluid and electrolytes, probably have had much to do with the lessened incidence of this grave postoperative complication.

SUMMARY AND CONCLUSIONS

In order to evaluate more properly the factor of anesthesia in acute gastric dilatation a comparative study was made of the effects of anesthetics on gastric tonus and motility in the trained dog. Studies were made on animals in which the extrinsic gastric nerves were present and after vagotomy and splanchnicectomy. The apparatus used to record the motor activity of the stomach was the balloon-bromoform manometer apparatus. The balloon was inserted into the stomach through a Mann-Bollman type of fistula.

It was found that anesthetics had either a depressing effect on gastric tonus and motility or no effect at all. The decrease in activity was in a general way directly proportional to the degree of anesthesia produced, regardless of the agent used. Anesthesia carried to plane 2 of the third stage by any of the inhalation anesthetics, whether employed alone, in combination with another inhalation anesthetic, or supplemental to a basal anesthetic of avertin with amylene hydrate, caused a marked reduction in gastric tonus and complete cessation of motility.

The effect of these anesthetics on gastric tonus and motility was essentially the same after splanchnicectomy or vagotomy or both, as was observed in the innervated animal. It was concluded that this effect was not mediated through the vagus or splanchnic nerves and was therefore primarily on the peripheral gastric motor mechanism.

There was very little evidence to indicate that the decrease in gastric tonus and motility was dependent on the relative quantity of oxygen in the blood and tissues during anesthesia.

A rather striking individual susceptibility to the depressing effect on gastric motor activity was exhibited by the dogs in this investigation. In some dogs there was a tendency for a quicker return of activity no matter what anesthetic was employed; in others a relatively greater time elapsed before tonus and motility returned to normal.

Premedication with morphine and atropine definitely prolonged the depressing effect of ether.

Apparently the depth is more important than the duration of anesthesia in relation to the effects on gastric tonus and motility. Increasing the duration of ether anesthesia fivefold prolonged the depressing effect very little.

No explanation is given for the decrease in gastric motor activity which was observed during spinal anesthesia.

The possible role of anesthesia in acute gastric dilatation as observed clinically is discussed.

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TRAUMATIC RUPTURE OF THE PREGNANT UTERUS RESULTING FROM AN AUTOMOBILE ACCIDENT

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IN THIS modern machine age, when more than thirty thousand persons annually meet their death in highway accidents in the United States alone, it is surprising to discover that traumatic rupture of the pregnant uterus from this cause has received practically no attention. Doubtless, many cases have not been reported in literature, but because of the rarity of this obstetrical calamity, and its numerous problems in diagnosis and treatment, the following case was thought to be of interest.

The scope of this paper is limited to those cases of traumatic rupture of the pregnant uterus from external violence alone. No consideration has been paid to spontaneous rupture, rupture through cesarean section or myomectomy scars, or to those uteri which were ruptured as the result of operative attempts at delivery or abortion, or as the result of obstructed labors.

A very complete review of the literature was made by Jaroschka in 1929,[1] and a series of forty cases of traumatic uterine rupture previously reported by Estor and Pueck were studied. To this series he added one case of his own from the Prague Clinic.

DeLee[2] reported one case in 1904, of a patient who fell on the steps striking her abdomen, which resulted in a ruptured uterus and dead infant. This patient recovered following operation some sixty hours later.

Orthner[3] reported another case in 1933, of a patient at term, who was struck across the abdomen by the beam of a trace attached to a team of horses. At operation one and one-half hours later a complete rupture of the uterus in the fundal portion was found, with twin boys lying free in the abdominal cavity. The edges of the laceration were sutured and she made an uneventful recovery.

Another case was added by Lazard and Kliman[4] in 1936, of a primipara, eight months pregnant, who fell down steps striking her abdomen on the edge of the steps. Severe abdominal pain was noted for one hour, later the pain being referred to the shoulder. This was followed by moderate vaginal bleeding and cessation of fetal movements. On admission to the hospital the abdomen was markedly distended, but fetal parts were clearly palpable beneath the skin. When the abdomen was opened the peritoneal cavity was found full of blood, with the fetus

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lying in the intact amniotic sac. The placenta had been completely separated from the uterus through a large rent in the posterior uterine wall. The uterus was firmly contracted. A supravaginal hysterectomy was done and the patient recovered.

Snidow[5] reported a similar case of multipara who had fallen down a flight of stairs. The patient stated that there was no pain immediately after the fall, but that one hour later she began having severe abdominal cramps and a slight amount of vaginal bleeding. Eight hours later there was a profuse vaginal hemorrhage followed by profound shock. At operation the abdomen was filled with blood with the fetus lying free in the abdominal cavity. There was a longitudinal tear in the midline posteriorly extending from the fundus of the uterus to the internal os. The placenta was adherent to the anterior uterine wall. This patient also made an uneventful recovery after supravaginal hysterectomy. It was found in reviewing this patient's past history that she had had a toxemia with her previous pregnancy, and a subsequent endometritis for several weeks after delivery.

One further case of ruptured uterus by indirect injury is given by Stapleton[6] from New Delhi, India, of a Hindu primipara, aged 17 years, at full term, who had fallen ten feet from a first floor veranda. The patient fell on her right side, being only stunned for several minutes. She stayed in bed for the next few days, had several episodes of nausea and vomiting, and complained of pain over the right hip and loin. Five days later she was again up and about and able to take food. According to the patient, fetal movements were felt three to four days after the accident. There was a slight bloody vaginal discharge for four days prior to admission. At this time the relatives said they did not think the baby was still alive because the abdomen was getting smaller. Examination showed a term pregnancy with the head in the left occipito-anterior position, at the pelvic brim. There were no fetal movements or heart tones. No abdominal distention or tenderness was elicited. Vaginal examination presented a long, closed cervix. Medical induction was attempted with castor oil, quinine, and enemas. After two days there were still no labor pains and only a moderate bloody "show"; the temperature was normal. The following day a piece of membrane was seen in the vagina, and the head bones of a macerated fetus could be felt above the internal os. At laparotomy a macerated fetus lying free among the intestines was removed. The placenta was located low down in front of a small, firmly contracted uterus, the edges still attached to a large, gaping, transverse tear across the fundus. The uterus had retracted and involuted in the shape of a cup. The peritoneal cavity contained a small amount of brown free fluid, but no signs of recent bleeding or general peritonitis. The rent in the uterine wall was hastily repaired and the wound closed with drains. The patient later developed pleurisy and pneumonia with a separation of the abdominal wound and fecal fistula. This subsequently closed and the girl recovered.

CASE REPORT

Mrs. J. J. (54,634) is a primipara, aged 20 years. She had the usual childhood diseases without complications, and an appendectomy through a McBurney incision in 1939. Her menstrual periods had been quite irregular since their onset at the age of 13 years, recurring every three or four weeks, but with normal flow of four to five days. She had had no serious illnesses, pelvic infections, or curettages. The patient's last menstrual period was on Feb. 6, 1940, making her estimated date of confinement Nov. 13, 1940. Fetal heart tones were heard at her regular ante-partum visit in July and August, and the uterus had enlarged normally, corresponding to the term of pregnancy. On September 7, she was riding in the front seat of a car driven by her sister-in-law, when they were involved in a head-on collision. The patient was thrown out of the right door, landing on her back at the side of the road. The car fell across the dorsal surface of her thighs, which were flexed upon the abdomen. The patient was not unconscious and was able to pull herself back into the car after it was lifted free. She was then carried to a passing car and brought immediately to the hospital. On admission she complained of severe upper abdominal pain "just as if everything was going to drop out." The temperature was 99.4° F.; pulse, 130; and respirations, 28. The blood pressure was 90/70, with 67 per cent hemoglobin, and 3,780,000 red blood cells. The abdomen was tender but not rigid, with no distention. The uterus was enlarged to the size of a seven months' pregnancy and fetal parts were not easily felt. There was no vaginal bleeding and no fetal heart tones were heard, but the patient stated that she felt fetal movements after her admission to the hospital. These were never detected by either the intern or the examining physician. A small laceration on the dorsal surface of the right thigh was dressed but no sutures were necessary. The patient was placed in Trendelenburg position and an ice bag applied to the abdomen. Intravenous fluid and a blood transfusion were given as quickly as possible. In two hours the blood pressure had risen to 112/84 and the pulse was 92. She still complained of abdominal pain but her general condition seemed improved. The possibility of uterine rupture was considered at this time, but in view of her rapid recovery on only supportive treatment, premature separation of the placenta with fetal death was thought to be a more likely diagnosis. There was still no external vaginal bleeding. Morphine was given for the abdominal pain. X-ray of the abdomen showed fractures involving the transverse processes of the five lumbar vertebrae on the right side, and fractures of the transverse processes of the fourth and fifth lumbar vertebrae on the left. A scout plate of the abdomen about ten days following the accident showed one fetal skeleton of about six months gestation with overlapping of the skull bones. The temperature during the first two weeks of hospitalization ranged between 99.6° and 101° F. and the pulse from 78 to 122. The patient continued to complain of some upper abdominal pain which was momentarily relieved with narcotics. The appetite remained good and the bowel function regular. Three weeks following the accident, when I saw the patient for the first time, pelvic examination revealed a long, firm, undilated cervix. There was no vaginal discharge or bleeding. On bimanual examination the uterus was felt to be about the size of a four months pregnancy and separated from a larger mass posterior and to the right. On Oct. 8, 1940, one month following the accident, a laparotomy was performed through a lower midline incision. The uterus and all pelvic organs were walled off by a fibrinous exudate. There were loops of bowel adherent to underlying pelvic structures. After these were separated the fetus was found lying free in the pelvic cavity, and there was a complete laceration of the uterus, extending down the posterior surface from the fundus to the cervix. The edges were ragged and widely separated, leaving a defect in the wall about 8 cm. in diameter. The placenta had been partially delivered through the laceration, but the cord was still firmly attached to the fetus. This tissue was extremely friable and broke into

many pieces when an attempt was made to remove it from the pelvic structures. Several pieces which were densely adherent to loops of bowel and the pelvic wall were left in situ. The fetus appeared well developed, about 40 cm. in length, but had undergone considerable maceration. There was no free fluid in the abdomen. It was found impossible to repair the rent in the uterine wall, consequently a supravaginal hysterectomy was done. The abdomen was closed in layers without drains. The postoperative course was complicated by a severe bronchopneumonia which was successfully treated with sulfapyridine. The patient was discharged from the hospital on the seventeenth postoperative day, only to be readmitted Nov. 26, 1940, with a partial intestinal obstruction. This was relieved with a Miller-Abbott tube. When last seen for her checkup examination June 2, 1941, she stated that she had been feeling well. Her appetite was good and bowel habits regular. The abdominal wound was well healed. There had been no vaginal bleeding or discharge. Pelvic examination showed the cervix to be clean and well suspended. The right ovary was palpable deep in the right fornix. The left fornix was clear. Rectal examination was negative.

Histologic study of the uterine muscle showed nothing abnormal except that the myometrium contained many highly dilated blood spaces. The muscle fibers were increased in diameter and somewhat tortuous from shortening. The endometrium was hypertrophied and densely infiltrated with small round cells. Buried in the endometrium were masses of necrotic placental villi.

DISCUSSION

It seems safe to assume that uterine rupture in this case occurred at the time of the accident due to the blow upon the abdomen. After the fetus and a portion of the placenta were extruded into the abdominal cavity, the uterus apparently clamped down very rapidly, allowing for only a minimal loss of blood. Fetal death must necessarily have taken place within several minutes following the accident. From the standpoint of diagnosis, this patient did not exhibit the usual signs associated with rupture of the uterus, namely, evidence of intra-abdominal hemorrhage, shock, accumulation of blood under the diaphragm, abdominal rigidity, pain radiating to the shoulder, or vaginal bleeding. The absence of these signs masked the true gravity of her condition, and led to the early mistaken diagnosis. It was only after the inflammatory reactions and toxic absorption were in evidence that operation seemed advisable.

Once the diagnosis of uterine rupture is made, the controversial question of whether to remove the uterus or to attempt a repair must be considered. The parity of the patient and desire for future pregnancies must necessarily influence our decision. If she is a primipara and is willing to gamble with the possibility of uterine rupture with subsequent pregnancies, preservation of the organ by suturing the laceration as effectively as possible may be in order. Many times this procedure is more time-consuming and hazardous than a rapid hysterectomy, especially when the patient is such a poor operative risk. Certainly, hysterectomy lessens the chances of infection and speeds the postoperative recovery. When the edges of the rent are widely separated and the

myometrium so extremely friable, as in the case reported, satisfactory uterine repair is impossible and hysterectomy must be done.

As has been mentioned by Orthner, traumatic lacerations of the uterus are due to a sudden increase in intra-abdominal pressure, which is transmitted to the uterus. The pregnant uterus, lying as it does, unprotected by the bony pelvic framework, is most prone to rupture in the fundal portion. This is the weakest point in the last trimester of pregnancy because of the vascularity of the uterine wall directly beneath the placenta.

Uterine rupture is designated as complete or incomplete depending upon whether or not the visceral peritoneum is opened. A complete laceration extends through the entire thickness of the endometrium, myometrium, and peritoneum, making a direct communication through the vagina to the peritoneal cavity. This is far more serious than the incomplete type in which the peritoneum remains intact. However, the maternal death rate in all types of uterine rupture ranges between 60 and 80 per cent, and reaches nearly 100 per cent for those cases not operated upon.

The classical sign of rupture of the pregnant uterus following severe abdominal trauma is evidence of bleeding, either external vaginal or intra-abdominal. This is accompanied by severe abdominal pain with tenderness and rigidity, usually of the rebound type. This denotes signs of peritoneal irritation from intra-abdominal hemorrhage. Very often a fluid level of blood in the peritoneal cavity may be outlined. If fetal parts are readily palpable directly beneath the skin, the diagnosis of uterine rupture should be suspected. These signs will be found accompanying those pointing to fetal death. In those cases exhibiting profuse external bleeding without signs of peritoneal reaction, accidental hemorrhage or placenta praevia must be thought of in spite of a history of abdominal trauma. In earlier pregnancy where signs of intraperitoneal hemorrhage are present, ruptured ectopic pregnancy or rupture of a poorly developed uterine horn may be the cause.

When uterine rupture occurs in the lower uterine segment, bimanual palpation for the round ligaments may give some clue to the diagnosis. On the side of rupture the ligament will be absent, while the opposite ligament may be readily palpable.

In spite of the satisfactory outcome of the case reported, the importance of early diagnosis and prompt operative treatment cannot be overemphasized, if the maternal mortality is to be reduced. The first and foremost effort should be exerted toward the control of shock by intravenous fluids and blood transfusions. This is frequently a life-saving measure until the patient's condition will warrant a laparotomy. Heroic efforts to control blood loss by clamping of the uterine arteries per vagina has been attempted by some men with success, while preparations for adequate surgery are in progress.

SUMMARY

1. Attention is directed to the rarity of traumatic rupture of the pregnant uterus from automobile accidents.

2. The salient points in the prompt diagnosis and treatment of this condition are briefly discussed.

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EPISPADIAS WITH INCONTINENCE IN THE MALE

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EPISPADIAS is fortunately, one of the rarest of congenital anomalies. Because of its rarity it is mentioned only casually in most urologic textbooks and in the past fifty years few articles dealing with this anomaly have appeared in the medical literature. However rare this condition may be from a statistical standpoint, to the individual so afflicted it is a tragedy, particularly if associated with urinary incontinence. The wet clothing and uriniferous odor resulting from this condition inevitably bring about social ostracism. This, together with the penile deformity, usually causes deep-seated psychic trauma. Most urologists see only a few such cases in a lifetime of practice. We must, therefore, rely in great part on both the successful and unsuccessful experiences of others in treating this malady.

Congenital epispadias is characterized by the abnormal location of the urethral opening on the dorsum of the penis. It may be situated anywhere from the glans penis to the penopubic junction and, depending on its location, epispadias may be classified as balanic, penile and complete, or penopubic. In contrast to hypospadias, the balanic type of epispadias is rarest, penile epispadias being slightly more common, and penopubic the commonest of the three. According to Hinman,[1] hypospadias occurs about 150 times as often as epispadias. As hypospadias is seen about once in every 300 or 350 males the incidence of epispadias is about one in 45,000 to 50,000 males. Nove-Josserand,[2] in fifteen years of urological practice, saw four cases of epispadias and sixty cases of hypospadias. Since the opening of the Duke University Hospital, approximately 168,000 patients, both male and female, have been seen. Among the male patients in this group there have been seventy-one cases of hypospadias and five cases of epispadias. All five cases were of the penopubic type, three having complete urinary incontinence and two having urinary control.

Complete epispadias is often associated with absolute incontinence of urine, which is due to a congenital lack of fusion of the internal and external urethral sphincters anteriorly. The sphincters and prostatic urethra may be so patulous as to easily admit the index finger. The symphysis pubis is characteristically separated, there being a heavy fibrous band of tissue joining the separated halves. The penis is of normal size or larger than normal and is drawn acutely upward to lie

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against the abdominal wall. The prepuce is redundant on the ventrum of the penis and lacking on its dorsum. The corpus spongiosum is absent and the corpora cavernosa are not firmly attached to each other but may be easily separated. The glans penis exhibits a defect or groove along its dorsal surface which is continuous along the dorsum of the penis with a depression between the corpora cavernosa which is lined with mucous membrane, an embryologic remnant of the urethral floor. This trough is continuous proximally with an infundibulum or funnel-shaped opening which extends inward beneath the symphysis pubis to become continuous with the prostatic urethra. The testicles are usually well descended and normal. The ejaculatory ducts are patent and ejaculation may occur into the bladder. The power of erection is usually present but coitus and procreation are virtually impossible. The bladder itself is normally formed and innervated but usually smaller than normal because of disuse. The internal vesical sphincter is widely dilated so that the interior of the bladder and prostatic urethra form a continuous pear-shaped cavity. The adjacent skin of the abdomen, thighs, and scrotum is often excoriated and infected from continuous soaking with urine.

The generally accepted embryologic explanation for the occurrence of epispadias and exstrophy of the bladder[3, 5, 6] is that there is a "cephalad displacement of the cloacal membrane in an early stage of development before the genital tubercle has made its appearance. The genital tubercle developing later arises below the cloacal membrane so that when the membrane is resorbed the urogenital sinus opens on the dorsum of the penis rather than on the ventrum. If the displacement of the cloacal membrane extends on to the primitive abdominal wall the result will be exstrophy of the bladder. If the displacement is of lesser degree epispadias alone results."

Two factors in the treatment of epispadias with incontinence must be considered, namely, correction of the urethral defect and cure of the urinary incontinence. The earliest surgical operations for this condition were directed toward the urethral defect. Thiersch,[7] in 1869, by means of skin flaps taken from adjacent tissues of the penis, scrotum, and pubis, was able to construct a urethra extending to the end of the penis and by application of a mechanical device which compressed the newly constructed urethra could produce artificial urinary control. This method was only partially successful due to the frequent formation of urethral fistulas. Cantwell,[8] in 1895, described his operation, which, modified, remains the operation of choice today for construction of the urethra. He noted the ease with which the corpora cavernosa could be separated in cases of epispadias. Utilizing the skin and mucous membrane of the dorsum of the penis he constructed a continuous urethral tube from the retropubic infundibulum to the tip of the penis. The corpora were then separated and the newly constructed urethra displaced to its proper position on the under surface

of the penis and held there by reapproximating the corpora dorsal to it. This procedure succeeded in creating almost normal relationship between the corpora cavernosa and the urethra, its greatest drawback being that sloughing of the newly constructed urethra occasionally occurred because of inadequate blood supply.

In 1918, Young[9] published his modification of the Cantwell operation which endeavored to avoid ischemia of the newly created urethra. The urethra was constructed from the skin of the dorsum of the penis, but left attached to one corpus cavernosum. After separating the corpora, the one to which the urethra was attached was rotated medially 180 degrees so as to carry the urethra to the under surface of the penis with its vascular connections to the rotated corpus still intact. Successful urethral constructions have also been reported by Barney,[10] Rockey,[11] and Cabot,[12] utilizing skin flaps from the prepuce, suprapubic region, or scrotum.

The experiences of these surgeons clearly established two points. Diversion of the urine, either by perineal urethrostomy, or preferably, by suprapubic cystostomy, is imperative for successful healing of the newly constructed urethra. If there is infection or excoriation of the skin of the penis, adequate time for its healing must be allowed after diversion of the urine before construction of the urethra is carried out. Secondly, the "splay" deformity of the penis must be corrected by resection of a portion of the dorsal skin and subcutaneous tissue and approximation by suture of the separated corpora.

Practically all the above authors noticed some degree of improvement in urinary control following simple construction of the urethra, although no correction of the sphincteric defect had been attempted. Page[13] and Bullitt[14] each reported a case of complete cure of urinary incontinence after simple construction of the urethra by Cantwell's technique. Some have stated that following construction of the urethra, if the sphincters are not too widely dilated, routine "sphincter exercise" may be sufficient to establish some degree of urinary control.

Duplay,[15] in 1880, recognized that the urinary incontinence in epispadias was due to a defect in the circular muscle fibers of the bladder neck. He cured one case of incontinence and greatly improved a second by partial resection of the dilated bladder neck and apposition of the cut edges by suture. Boiffin,[16] in 1895, after dissections on an epispadiac cadaver, pointed out that the defect in the internal sphincter was mainly in its anterior portion, and that adequate muscle for urinary control was present in these cases if it could be united. He stressed the importance of removing the anterior defective portion of the sphincters rather than the posterior segment which contained the bulk of sphincteric muscle and reported one case successfully cured of incontinence.

In female epispadias, plication, with or without torsion of the urethra, has been carried out with rather indifferent success, although Gautier[27]

reports cure of two cases by this technique. Muscles from other portions of the body have been transplanted and utilized for an artificial urethral sphincter by Deming,[17] Thompson,[18] and others. The gracilis, pyramidalis, rectus abdominis, and gluteus muscles have all been used for this purpose, a few cases of incontinence having been cured by each of these procedures.

In 1906, Trendelenberg[19] advocated excision of a broad, wedge-shaped portion of the anterior and lateral walls of the infundibulum from below, reuniting the defect with sutures. If incontinence persisted he operated again and excised more of the urethra and external sphincter. If the infundibulum were very large with some protrusion of the bladder wall through it, he divided the intersymphysial ligament and resected the roof and lateral walls of the prostatic urethra as well as a portion of the bladder neck, reapproximating these structures with sutures. He stressed the importance of reuniting the symphysis pubis with buried silver wire sutures and reported cures of incontinence in two cases.

In 1922, Young[20] described his double sphincter operation for the cure of epispadias with incontinence. The details of this operation are well known and consist of suprapubic cystotomy with excision of an appropriately large wedge-shaped piece of tissue from the roof of the prostatic urethra and the anterior portion of the vesical orifice. The cut edges are reapproximated by means of continuous suture, so as to draw together and tighten the prostatic urethra and internal vesical sphincter. The intersymphysial band is not divided but the roof and a portion of the lateral walls of the infundibulum and the anterior portion of the external sphincter are excised from below. These raw edges are likewise reapproximated by continuous suture, thus tightening the external sphincter and bulb of the urethra. In 1940, Dr. Young[21] reported thirteen cases of epispadias with incontinence on whom this operation had been performed with creation of complete urinary control in twelve cases and almost perfect control in the other. Muschat,[22] in 1927, reported three cases of epispadias with incontinence cured by Young's operation. Other cures have been reported by Cecil,[23] Lowsley and Kirwin,[24] Hinman,[1] and others.

Exstrophy of the bladder at the present time is usually treated by transplantation of the ureters into the sigmoid. Some[25, 26] have advocated this as the procedure of choice in epispadias with incontinence. Others have resorted to its use only after plastic operations on the vesical sphincters have failed.

Since the opening of the Duke Hospital five patients with epispadias have been seen, three of whom had complete urinary incontinence. One of these three patients refused operation. The other two patients were operated upon and excellent results were obtained.

CASE 1 (Duke Hospital No. 59615).—H. R. S., a 14-year-old white boy, was admitted on the Urological Service, Oct. 15, 1935, complaining of urinary incon-

tinence and deformity of the penis since birth. The past health had been excellent. There had been occasional excoriation and infection of the skin around the genitalia but nothing to suggest upper urinary tract infection; erections had been frequent. When the patient was at the age of two or three years, his physician had removed a portion of the prepuce without influencing the urinary incontinence. At the time of admittance he was in the seventh grade of school. He wore cotton pads to protect his clothes from the dribbling urine; although there was constant dribbling, on occasions the child would void a considerable amount, varying from 50 to 100 c.c. but immediately afterward urinary dribbling would continue.

General physical examination was negative except for a well-compensated rheumatic heart disease. The penis presented a classical picture of complete epispadias with incontinence (Fig. 1), measuring 4 cm. in length and being broad and thick. Urine constantly seeped from the retropubic infundibulum. Intravenous urograms and plain x-ray showed a normal upper urinary tract and some separation of the symphysis pubis.

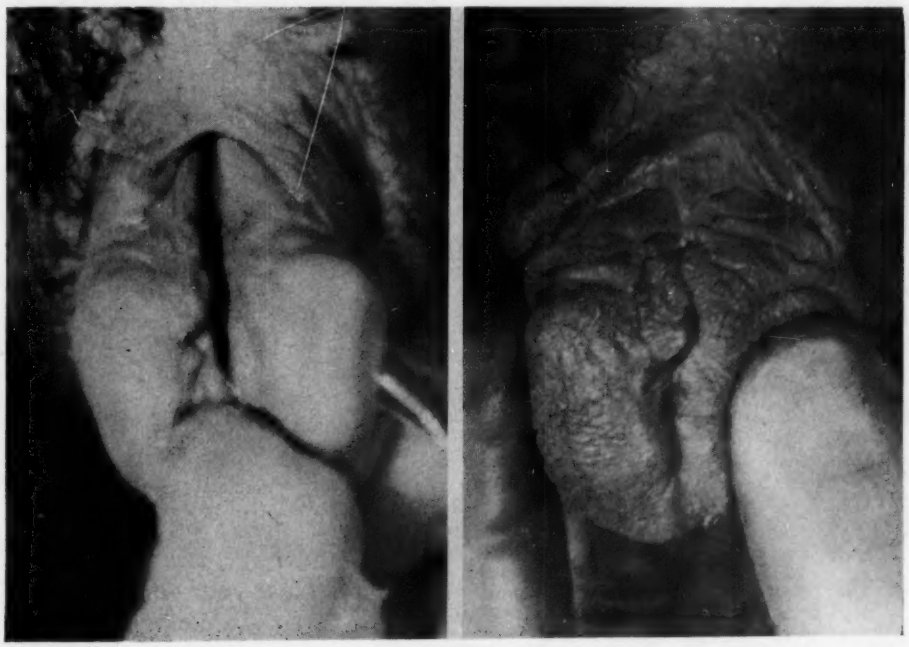

Fig. 1 (Case 1).—Epispadias with incontinence; appearance of penis before and after operation.

On Oct. 23, 1935, the bladder was opened suprapubically and found to be large and atonic. The internal sphincter was relaxed. Young's double sphincter operation was carried out in two stages, the repair of the internal vesical sphincter being done at this time and construction of the urethra carried out, Dec. 2, 1935. Convalescence from both procedures was uneventful, the urethral repair healing per primam. The patient was discharged Jan. 25, 1936, voiding normally from the new urethral meatus without incontinence. On Sept. 8, 1941, almost six years after operation, the patient reported by letter that he was doing heavy manual labor and that urinary control was perfect.

Case 2 (Duke Hospital No. A57641).—J. E. B., a 15-year-old boy, was admitted on the Urological Service, March 11, 1941, complaining of deformity of the penis and constant dribbling of urine since birth. No attempts at surgical correction

of the deformity had been made, nor had any apparatus or dressing been used to collect the urine. The boy had never been to school and was shunned by other children. There was nothing in the past history to suggest upper urinary tract infection. Occasionally there had been fairly firm erection, but there was no history of ejaculation or orgasm.

Examination disclosed a tall, shy, undernourished boy of fifteen. His clothing below the waist was soaked with malodorous urine. Over the thighs and lower abdomen were numerous furuncles. The penis showed complete epispadias with incontinence (Fig. 2) and the examiner's finger could easily be passed through the infundibulum into the bladder. The corpora cavernosa were easily separable along the proximal half of the shaft of the penis, distal to which point they were firmly attached together. At the summit of the glans was a small dimple, through which, on subsequent investigation, sounds could be passed into a false urethra along the under surface of the corpora. This terminated blindly beneath the

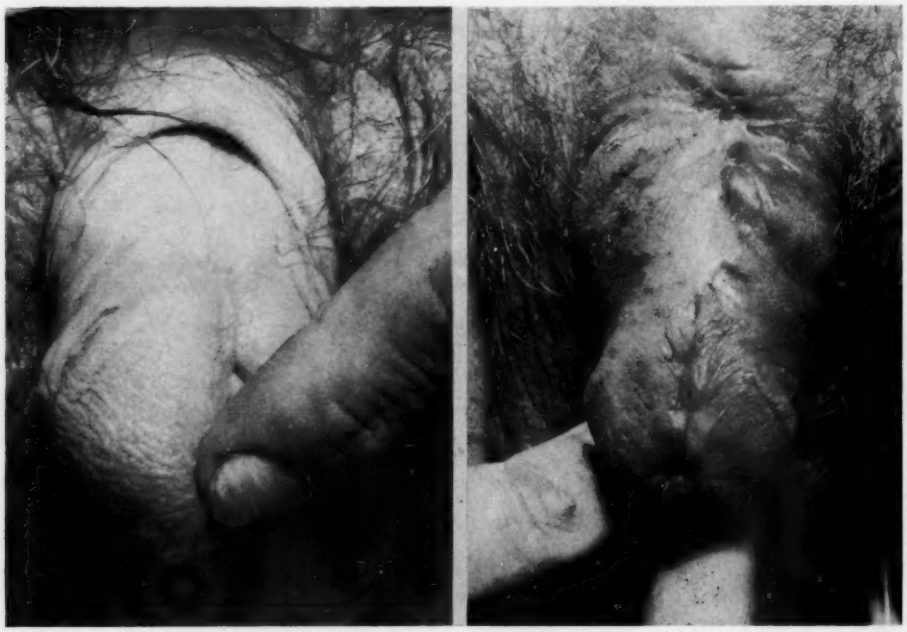

Fig. 2 (Case 2).—Epispadias with incontinence; appearance of penis before and after operation.

mucous membrane covering the dorsal groove of the penis just proximal to the point of separation of the corpora. Both testicles were descended and of normal size. Rectal examination disclosed a prostate of average size for a 15-year-old boy. On cystoscopy the bladder wall was normal, the bladder capacity being 130 c.c. There was no evidence of cystitis. The trigone was indistinct and difficult to delineate. With very little fluid in the bladder, a relaxed internal vesical sphincter could be visualized, but on partially filling the bladder this region was completely smoothed out, the bladder wall appearing continuous with the prostatic urethra. The verumontanum was prominent and both the utricle and left ejaculatory duct were easily seen. No definite external urethral sphincter could be demonstrated. Plain x-ray and intravenous urograms showed a normal upper urinary tract. The urine was normal and uninfected.

On March 17, 1941, a modification of Young's operation for epispadias with incontinence was carried out. The procedure differed from Young's classical operation in several technical points which we feel are worthy of recording. The

bladder was exposed by a generous midline incision, but prior to opening, its anterior and lateral walls, as well as the anterior and lateral surfaces of the prostate, were completely freed by blunt dissection down to the triangular ligament. The puboprostatic ligament was easily broken with the dissecting finger. The bladder and prostatic urethra were opened along the midline anteriorly down to the external sphincter. Since the internal vesical sphincter could not be identified as such, a point was arbitrarily chosen halfway between the verumontanum and interureteric ridge for the new bladder neck. A triangular piece of bladder wall and prostate was then removed from each side of the midline (Fig. 3). The incisions were so placed that the base of each triangle was represented by the midline incision through the bladder and prostate and the apices of the triangles lay about 8 mm. apart at the level chosen for the internal vesical sphincter. The

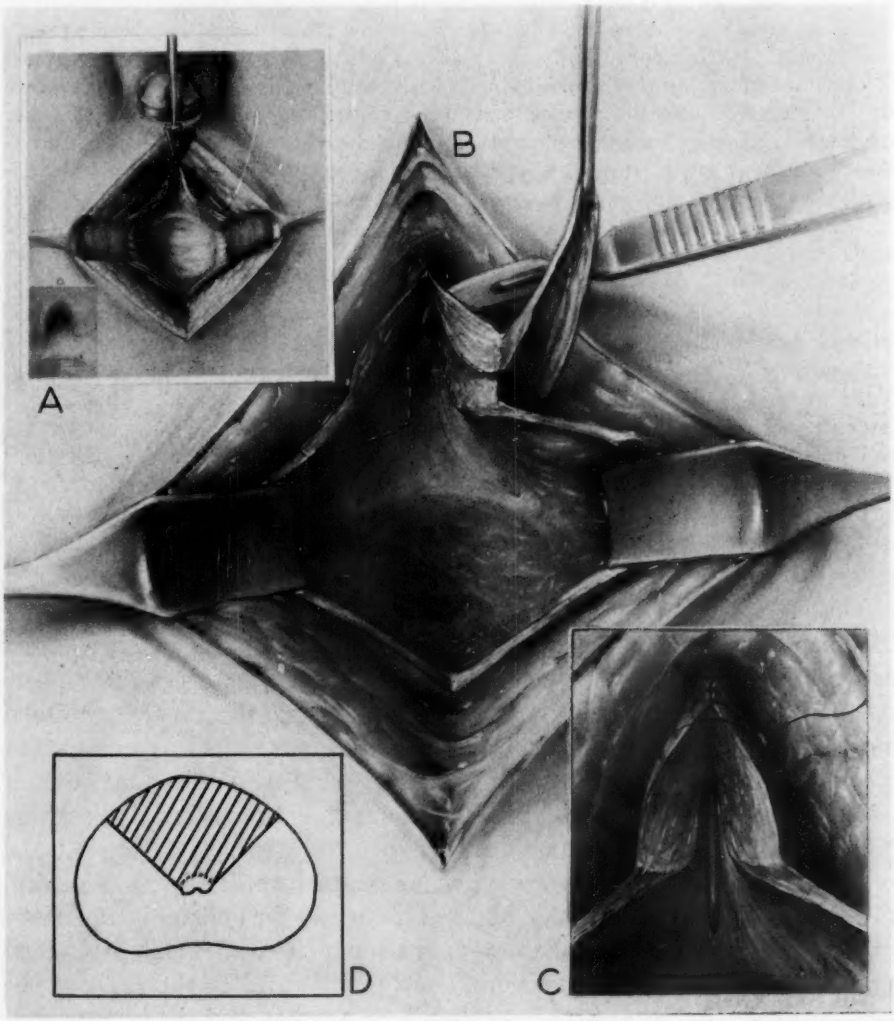

Fig. 3.—*A*, Young's technique for resection of wedge from vesical neck and prostatic urethra. *B*, Bladder and prostatic urethra opened along midline to membranous urethra, resection of triangular piece of tissue from roof and right lateral lobe of prostate and adjacent bladder; cut edges of floor of prostatic urethra are parallel and closure results in snug internal sphincter and tubular, rather than conical urethra; corresponding tissue is excised from left side as indicated in illustration. *C*, Closure results in tubular urethra, tight internal sphincter; second layer of plicating sutures to be introduced. *D*, Cross section of prostate shows preservation of only floor of urethra but of most of lateral prostatic lobes by oblique incisions.

incisions through the prostatic tissue were made obliquely, preserving a strip of mucosa along the floor of the urethra, 8 mm. in width, and the greater portion of the lateral lobes of the prostate. The prostatic urethra was then closed over a No. 8 French soft rubber catheter in two layers, the first layer of sutures snugly approximating the structures, the second layer plicating the prostatic urethra and internal sphincter. The bladder was closed around a mushroom catheter with chromic catgut, the wound closed and drained routinely. The lateral walls and roof of the infundibulum as well as the anterior segment of the external sphincter were then excised from below according to Young's technique. The mucosa and periurethral tissues were closed over the catheter with fine chromic catgut.

Following removal of the suprapubic catheter on the seventeenth day, urinary control was rapidly established and by the thirty-eighth postoperative day was almost perfect. On this date the bladder was reopened and drained suprapubically. A No. 16 sound was introduced into the false urethra and its tip forced through the mucosa covering the dorsal groove of the penis. A relatively short segment of urethra connecting the infundibulum with the proximal end of the false urethra was constructed from the mucous membrane of the dorsum of the penis. After the anastomosis was completed the proximal halves of the corpora were separated, the newly constructed urethra displaced ventral to them and held there by re-approximating the corpora with chromic catgut sutures. A longitudinal segment of skin and fibrous tissue was excised from the dorsum of the distal half of the penis and glans, the defect being closed with vertical mattress sutures of fine silver wire.

Convalescence was uneventful, the urethral construction healing per primam without fistula. At the time of discharge, May 27, 1941, the patient was voiding with perfect urinary control during the day, but having slight incontinence at night while asleep. The operative incisions were completely healed. Five months later the patient could retain urine for more than four hours and had perfect control during both day and night except for very occasional enuresis. Erections had been frequent but intercourse or masturbation had not been attempted. The urine was normal and the urethra easily accommodated a No. 16 French sound.

COMMENT

The embryologic vagary responsible for the concomitant occurrence of epispadias and an essentially normally placed false urethra offers room for speculation. According to Bremer[3] and Arey,[6] the cloacal membrane originally extends from the tail bud to the future umbilical cord. Normally, by the time the genital tubercle has appeared, the cloacal membrane has receded so as to cover only the caudal surface of the tubercle and the perineum forming the urogenital sinus which later closes to form the urethra. Failure of recession of the cloacal membrane from the lower abdomen or ventral surface of the genital tubercle results in exstrophy of the bladder or in epispadias. In our case, it seems probable that there was a separation of the cloacal membrane into two portions, one dorsal and one ventral to the crest of the genital tubercle, the former resulting in epispadias and the latter forming the terminal portion of the pendulous urethra. It is interesting to note that the corpora cavernosa were firmly attached together along that segment of the penis traversed by the false but normally located urethra, whereas proximal to the false urethra they were considerably separated.

DISCUSSION

There is, of course, no way of accurately estimating the percentage of cure of epispadias with incontinence by plastic operation on the vesical sphincters and urethra. The operative result, naturally, will be governed by the operative technique employed, the surgeon himself, the amount of sphincteric muscle available for approximation, wound infection, and a host of other factors. As with many surgical procedures, operative failures are much less frequently reported than are successes. It seems significant, however, that in all reported groups of cases, almost without exception, the urinary incontinence was either completely cured or very greatly improved after partial resection and reapproximation of the vesical sphincters. If the outcome of operation is successful, these individuals are restored to a completely normal social state and to a practically normal physical condition. Coitus is usually quite satisfactory, moderate upward curvature of the penis being much less of a handicap than a corresponding degree of ventral chordee. Urinary infection, if present, presents no different therapeutic problem than it does in a normal individual. The upper urinary tract has not been disturbed and the life expectancy of the individual should not differ from the average at his age. This is in distinct contrast to the conditions obtaining after ureteroenterostomy, where chronic renal infection is almost the rule. The great value of ureteral transplantation to the bowel is unquestioned in certain incurable conditions, such as exstrophy of the bladder, and vesical carcinoma. In epispadias with incontinence, however, where the abnormality is curable in a fairly high percentage of the cases, we feel that the advantages of plastic repair so far outweigh those of ureteroenterostomy that the latter should be reserved as a procedure of last resort.

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A NEW SKIN VARNISH FOR MAINTAINING STERILITY OF THE OPERATIVE FIELD

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ALTHOUGH avoidable infections of operative wounds may be expected to take place as long as operations are performed, surgeons will always strive to minimize them. The percentage of infections in clean surgical wounds is still significant.[1] This paper is not concerned with bacteria which may be in the air, on contaminated instruments, or on the hands of the surgical personnel but only those on the skin of the operative field.

It has been abundantly demonstrated that the tissues surrounding a wound cannot be completely sterilized by any methods now in use. Bacteria which remain deep in the sweat and sebaceous glands are washed out with perspiration and are readily swept into wounds by instruments or the hands of the surgeon.[2] Because of this danger, many surgeons protect the edges of the wound with skin towels through which, however, perspiration or other fluids may soak. Some surgeons apply antiseptics or bacteriostatic agents just before closing the wound. It is debatable what percentage of wound infections can properly be ascribed to contamination with organisms from the contiguous skin but proper provision should be made to minimize this risk.

Rubber gloves[3] are worn almost universally now to protect the wound from bacteria on the surgeon's hands. Since it is just as impossible adequately to sterilize the human abdomen as it is to sterilize the human hand,[4] there have been many attempts to isolate the operative field by means of impervious materials, such as silk dipped in celloidin,[3] rubber sheets, and various waxes.[5, 6] None of these methods has come into general use.

Accordingly, a preparation has been devised at my request by Mr. Carl Bauer, a research chemist. This substance is a cellulose product which is dissolved in a mixture of ether and alcohol and is referred to as skin varnish.* It is self-sterilizing and can be sprayed or painted on the skin of the operative field forming an impervious coating which is insoluble to water but which, unlike collodion, can easily be redissolved at the end of the operative procedure. This preparation is

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*The skin varnish, known as Surgical Skin Varnish, is available for investigational use on application to E. R. Squibb & Sons. The formula is as follows: ethyl cellulose, 165.0 Gr.; acetone, 605.0 Gr.; ethyl alcohol, 715.0 Gr.; butyl lactate, 22.0 Gr.; castor oil, 16.5 Gr.; and santicizer B-16 (Monsanto), 16.5 Gr.

chemically inert and does not react with iodine or other common antiseptics. The solute is noninflammable, nontoxic, nonexplosive, nonirritating, and does not interfere with healing of wounds or with making an incision. It merely provides an impermeable, pliable, transparent coating over the skin of the operative field which prevents organisms in the skin excretions from being wiped into the wound.

LABORATORY RESULTS*

Bacterial cultures of the varnish in both aerobic and anaerobic media revealed no growth of organisms.

Seventeen male patients on the medical wards of the Syracuse University Hospital were used in testing the preparation in the following manner (a modification of the method of Novak and Hall[7]). Sterile watch glasses containing a nutrient blood agar medium were strapped with the medium next to the unprepared skin of the four abdominal quadrants and allowed to remain for fifteen minutes. These were then removed and incubated for twenty-four hours at 37° C. and the colonies of microorganisms identified and counted. Immediately following the removal of these watch glasses the entire abdomen was shaved, scrubbed for ten minutes with surgical soap, washed with 70 per cent alcohol (by weight) and ether. The two lower quadrants then received two applications of 1 per cent iodine, which was allowed to dry and then removed with 70 per cent alcohol. The two quadrants on the patient's right side were then sprayed with the varnish, approximately 5 to 8 c.c. being used for each case. After the varnish dried, a matter of one or two minutes, the bacteriologic medium was applied to the skin of each of the four abdominal quadrants as previously described. A cradle containing four 40-watt electric light bulbs was placed over the abdomen, the bed clothes were drawn over this and allowed to remain for forty-five minutes. Marked perspiration occurred in each case. The watch glasses were then removed, incubated, the bacteria identified, and the colonies counted. Thus, of the four abdominal quadrants all of which were cleansed with soap, alcohol, and ether, one quadrant was a control, one received only iodine, one only varnish, and one both iodine and varnish before being subjected to heat.

The unprepared abdomen contained a minimum of 260 colonies and an average of 1,231 colonies per watch glass (an area of 33.1 sq. cm.), and there were about the same number of organisms in each quadrant of any given abdomen. The most common organisms were the *Staphylococcus albus* and diphtheroid bacilli. The abdominal quadrant that was only cleansed before being exposed to heat contained an average of seventy-seven colonies per watch glass. The use of iodine, varnish, or both resulted in there being, respectively, an average of twenty-five, three, or one colony per watch glass. Thus, the best results were obtained

*The laboratory studies were carried out by Ralph W. Getty, under the direction of Dr. O. D. Chapman.

when both iodine and varnish were used. Under these circumstances, eleven of seventeen cases were completely sterile and there were never more than six colonies per watch glass.

In the skin that was only cleansed there were four instances in which more than 100 colonies were present but in the other thirteen instances there were never more than ten colonies. When iodine alone was used there were two cases of the seventeen where two hundred colonies were found. However, when the varnish was used with or without iodine there were never more than ten colonies per watch glass. These observations suggest that it is only the occasional patient who has a significant number of organisms in the depths of the sweat and sebaceous glands of the abdominal wall. These patients may be especially likely to suffer from wound infection.

CLINICAL RESULTS

The varnish has been used in forty major operations since July 9, 1940. There were seven laparotomies, sixteen laminectomies, and seventeen craniotomies. The skin was usually prepared with soap and water, ether, alcohol, and iodine. In one case the patient was sensitive to iodine and merthiolate was used as the antiseptic agent. The varnish was applied with a sterile sponge or with an atomizer* so that a thin coating lay on the skin of the operative field. If wound towels were used in addition to the coating and were rubbed firmly over the skin, the varnish was scraped off. Otherwise, the coating was intact at the end of the procedure, when the varnish was removed with a mixture of alcohol and ether.

In no case was there irritation of the skin or any interference with healing of the wound. There were two cases of low-grade infection of the wound following removal of a gangrenous appendix, and one following an umbilical hernioplasty. There was one wound infection following hemilaminectomy in a man 73 years of age. The other thirty-six wounds healed by primary intention. The percentage of infection in these cases is without significance because suitable controls were not available.

Other possible uses of this product, perhaps combined with sulfonamide drugs, in the treatment of burns or chronic ulcers of the skin, and in protecting the skin from noxious discharges and chemical agents should be investigated. It has been used with encouraging results on a persistent bed sore. Because it can be redissolved so easily it may prove to be superior to collodion for many other uses.

CONCLUSION

A new skin varnish fills a theoretic need for preserving sterility of the skin in the operative field. Its value has been confirmed by counts of bacteria on the human abdominal skin under conditions similar to

*The atomizer was supplied by the deVilbiss Co., Toledo, Ohio, and is similar to that used to spray tannic acid.

those of laparotomy. The varnish does not delay the operation, irritate the skin, or interfere with wound healing. It will not be possible to judge the practical value of this preparation in preventing postoperative infection until it is used in a large number of operations with suitable controls. It is in the hope that such investigations will be carried out in some of the larger surgical clinics that this preliminary report is presented.

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A CONSIDERATION OF THERAPY IN STAPHYLOCOCCUS INFECTIONS

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SOME of the most important factors in any consideration of therapy in staphylococcal infections are first, the variations in the bacteria; second, the influence of extrinsic factors on the organism; and third, the dual nature of some staphylococci. There are some staphylococci that show many toxigenic activities similar to those of the diphtheria bacilli and also, the invasive characteristics of certain streptococci. Each of these factors deserves consideration from a therapeutic standpoint.

Reviews recently published discuss many of the characteristics of the staphylococci. Among these is one by Blair[1] in which he reviews the problem of the pathogenic staphylococci. In this he considers the toxin, the coagulase, and the fibrinolytic properties of the staphylococcus. The differentiation of the pathogenic from the nonpathogenic staphylococci is discussed, and the classification of these organisms based upon the agglutinin and precipitin reactions. Blair[1] concludes that "the past several years have witnessed definite advances in knowledge of the staphylococci particularly with regard to their soluble toxic substances. . . . The exact relation of the toxins to the pathogenesis of staphylococcal infections demands further study."

Chapman and his associates,[2] in a paper entitled "The Differentiation of Pathogenic Staphylococci from Nonpathogenic Types," discuss in detail the various laboratory procedures used in the study of staphylococci, such as pigment production, hemolysis, coagulase, and the fermentation reactions. These investigators emphasize the difficulties that may arise in any study of staphylococci resulting from the development of variants in the cultures. They conclude that "the coagulase test is the most reliable single test for the differentiation of pathogenic from nonpathogenic staphylococci. When used in conjunction with pigment and coagulase tests, hemolysis of rabbit blood agar permits simple estimation of the degree of pathogenicity of a strain or variant." In view of the simplicity of technique by which hemolysis may be studied on rabbit blood agar media as compared with the technique for the coagulase test it would appear that the former test would be of greater value in the separation of pathogenic from nonpathogenic staphylococci.

Flaum,[3] in 1938, while reviewing the entire problem of the staphylococcus, considered at length that of immunity. He states that "in recent years the therapy of staphylococcus infections has been taken up with

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greater eagerness and enthusiasm perhaps than ever before and results have been published by various workers which seem to justify the enthusiasm with which they have been made known. The new feature of the methods which have been brought into use is that staphylococcal toxin as a rule in the form of toxoid, and serum, containing staphylococcal antitoxin, constitute the new weapons in the therapeutic arsenal, the purpose of which is to produce an active or passive immunity against staphylococci and their products.''

Rigdon,[4] in 1937, reviewed the problems of staphylococcal immunity in both man and experimental animals. From this paper there appears to be unquestionable evidence to indicate that staphylococcal antitoxin antibodies may play a very important role in the mechanism of the resistance of both man and experimental animals to staphylococcal infections. Staphylococcal toxoid would appear to be the antigen of choice in the immunologic treatment of skin infections. Staphylococcal antitoxin is of value in the treatment of certain acute cases of staphylococcal infections, especially those in which the clinical manifestations of toxemia are greater than one would expect from the number of bacteria present in the blood stream.

In a second review on staphylococcus toxin Rigdon[5] points out that evidence from the literature indicates that the toxin produced by certain staphylococci consists of a single toxic substance. There is insufficient data, he thinks, to prove that the lysis of red cells, the necrosis of epithelial cells in the skin, the destruction of white blood cells in the circulating blood, and the development of renal necrosis following an intravenous injection of staphylococcus toxin are the result of the action of four different toxic substances, each given off by the organism in the same preparation of filtrate. Rigdon considers that each of these pathologic lesions represents only a variation in the effect of a single substance reacting upon different tissues. If this concept is correct, then the use of one antitoxin would suffice to neutralize all the different effects produced by staphylococcus toxin. Rigdon has demonstrated that each of the so-called ''fractions'' in staphylococcus toxin was destroyed by the same agents. In these experiments the toxin was detoxified by several different methods and in each the hemolysin decreased at a rate comparable to the rate of destruction of the so-called ''skin necrotizing factor.''[6, 7]

The frequency in which studies on staphylococci are being published would indicate a growing interest in the morbidity and the mortality of such diseases as osteomyelitis, skin infections, food poisonings, and septicemia. They also indicate the need for diligent investigation of the staphylococcus and the therapy to combat it.

A simple technique for the classification of staphylococci would be valuable in any consideration of therapy. Blood agar media may contribute much in the separation of pathogenic and nonpathogenic staph-

ylococci. It is important to remember, however, that the red blood cells from different species are lysed at different rates by staphylococci. Gross[8] gives the order of susceptibility of the red blood cells from different species to staphylococcus toxin as follows: rabbit, ox, sheep, goat, man, guinea pig, and horse. One of us (R. H. R.) has observed a similar order of susceptibility of red blood cells to staphylococcus toxin: rabbit, goat, cow, cat, pig, rat, dog, mouse, monkey, turtle, sheep, man, horse, chicken, and guinea pig. In view of these observations it is important to know the type of red cell used in any blood agar media since the presence of a zone of hemolysis around staphylococcus colonies is considered to indicate a more virulent organism than a strain of staphylococcus that fails to produce hemolysis.

Antitoxin may be one of the factors in blood agar media that accounts for the failure in the development of this hemolytic zone about the colonies of hemolytic staphylococci. Staphylococcus antitoxin added to blood agar media inhibits the hemolysis produced by hemolytic staphylococci growing on the surface of the same plates.[9] This in vitro demonstration of the neutralization of the toxin by the antitoxin would suggest that a similar effect might occur in vivo.

Hemolysis is only one of the destructive processes resulting from staphylococcus toxin. De Christimas,[10] in 1888, demonstrated the necrotizing action of this toxin on the skin of laboratory animals. More recently pathologic changes in man have been attributed to staphylococcus toxin. Extensive necrosis of the mucosa in the lower ileum and first portion of the colon has been observed in a child dying with a staphylococcus septicemia. The primary infection in this case was in the middle ear and the organism was hemolytic. This intestinal lesion was attributed to staphylococcus toxin since a similar lesion was reproduced in the rabbit's colon by the intravenous injection of staphylococcus toxin.[11] Tubular and glomerular lesions also have been observed in cases of staphylococcal infection in man and similar lesions have been produced with toxin in experimental animals.[12, 13] Fig. 1 illustrates the necrotizing process that may be associated with the development of staphylococcal abscesses in the heart in cases of septicemia. Acute necrotizing ulcers in the skin have been attributed to the action of toxin liberated by the staphylococcus since a toxin producing organism was isolated from the lesions.[14] Pathologic lesions resulting from staphylococci have been described in cases of cavernous sinus thrombosis. The similarity of this lesion to that occurring in the small blood vessels of the rabbit's ear following the intravenous injection of staphylococcus toxin was demonstrated by Stookey and Scarpellino.[15] The coagulation of the tissue that may follow the local injection of staphylococcal toxin in experimental animals resembles the lesions that may occur in certain of the viscera following the intravenous injection of the same filtrate. The degree of injury may be influenced by the type of cell and con-

centration of the toxin in the cells. The union of the toxin with the cell apparently is rapid and irreversible. In all pathologic conditions in which the staphylococcus is the etiologic agent, toxin may account for a considerable part of the clinical and pathological picture.[14]

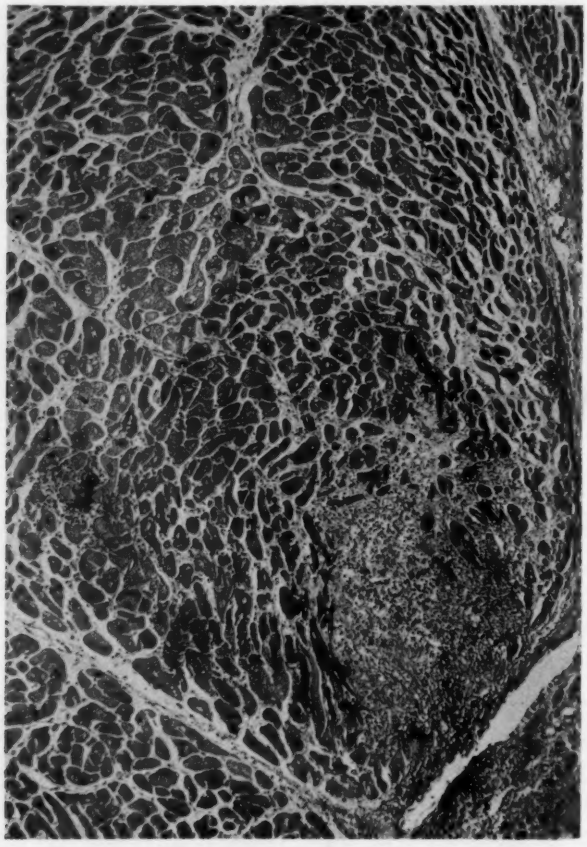

Fig. 1.—The cardiac muscle surrounding the abscess is degenerated, the type of necrosis may be classified as coagulation necrosis; this is the type of injury produced experimentally by staphylococcus toxin. The patient, a 44-year-old white female, had a *Staphylococcus aureus* septicemia.

The pathologic changes that occur in the subcutaneous tissue of mice are different following the subcutaneous injection of toxin and nontoxin-producing strains of staphylococci. In the former there is a diffuse spread of the bacteria and extensive necrosis; in the latter there is essentially no necrosis and complete localization of the bacteria after a period of approximately eight hours.[16] These observations on the effect of toxin and nontoxin-producing strains of staphylococci on tissue indicate that toxin is one factor that must be remembered in considering therapy in all cases of staphylococcal infections.

STAPHYLOCOCCUS ANTITOXIN

It would appear only logical to consider the use of a therapeutic agent in those cases of staphylococcal infections in which a toxin-producing

organism is present that will neutralize the toxin liberated by the bacteria. Experimental and clinical studies have been made to study the effect of staphylococcus antitoxin on the lesions produced by different strains of staphylococci and staphylococcal toxin.[16-23] This antitoxin when given to rabbits prevents the acute death that follows the intravenous injection of staphylococcal toxin. The histologic reaction that occurs in the subcutaneous tissue of mice following the local injection of a toxin-producing strain of staphylococci is essentially the same as that which occurs when a nontoxin-producing strain of staphylococci is injected subcutaneously if the animals are given staphylococcus antitoxin preceding the injection of the bacteria.[16]

Staphylococcus antitoxin and the results of its clinical use in the treatment of staphylococcal infections apparently was satisfactory, for the Council on Pharmacy and Chemistry of the American Medical Association accepted it in August of 1940.[25] The following two cases illustrate the use of staphylococcus antitoxin in the treatment of staphylococcal septicemia.

CASE 1.—A 4-year-old white female entered the hospital on July 20, 1939, with vesicular blebs over her neck, face, and scalp. These varied in size from 0.5 to 1.5 cm. in diameter and were 0.5 cm. in height. They were filled with a clear amber colored serous fluid; cultures from these blebs showed a hemolytic *Staph. aureus*. A blood culture taken on the second day of hospitalization was also positive for a hemolytic staphylococcus. It showed both aureus and albus colonies. A third blood culture taken on the seventh day of hospitalization, however, was sterile after seven days of incubation.

The temperature, pulse, and respirations for the six days following admission are shown in Fig. 2. The child, on the fourth hospital day, was given 100,000 units of staphylococcal antitoxin intramuscularly over a period of ten hours. An additional intramuscular injection of 20,000 units of antitoxin was given on the fifth day. The child was much improved on the sixth day. A small transfusion was given at this time; the temperature was 101° F. She continued to improve and was dismissed on the twenty-fifth day of hospitalization.

CASE 2.—E. P. A 23-year-old white female observed that her breasts were sore following the nursing of her baby. When she entered the hospital the right breast was very tender and the upper outer quadrant was firm. She had a severe chill and a rise in temperature during the evening of her first day in the hospital. A blood culture taken at this time was positive for a hemolytic *Staph. albus*. Ten grams of sulfanilamide were given to her on the second day of hospitalization. On the third day 50,000 units of staphylococcus antitoxin were given in 800 c.c. of a 10 per cent solution of glucose. This amount of antitoxin was repeated twenty-four hours later.

The patient felt much better on the fourth day. A blood culture taken at this time was sterile after seven days of incubation. A serum reaction occurred on the ninth day following the injection of the antitoxin. The patient improved and was discharged on the fifteenth day following hospitalization.

The dose of staphylococcus antitoxin always should be an amount sufficient to produce an excess of antitoxin in the circulating blood. The minimum dose should be 100,000 units preferably given intravenously.

In severe infections with profound toxemia, 300,000 to 400,000 units of antitoxin may be required. This foreign protein is rapidly eliminated from the body. It is usually absent from the blood in five to seven days. Parrish has demonstrated a simple technique for titrating the antitoxin (antihemolysis) in the serum of patients.[26] There is no method at this time by which the quantity of staphylococcal toxin in the blood may be determined.

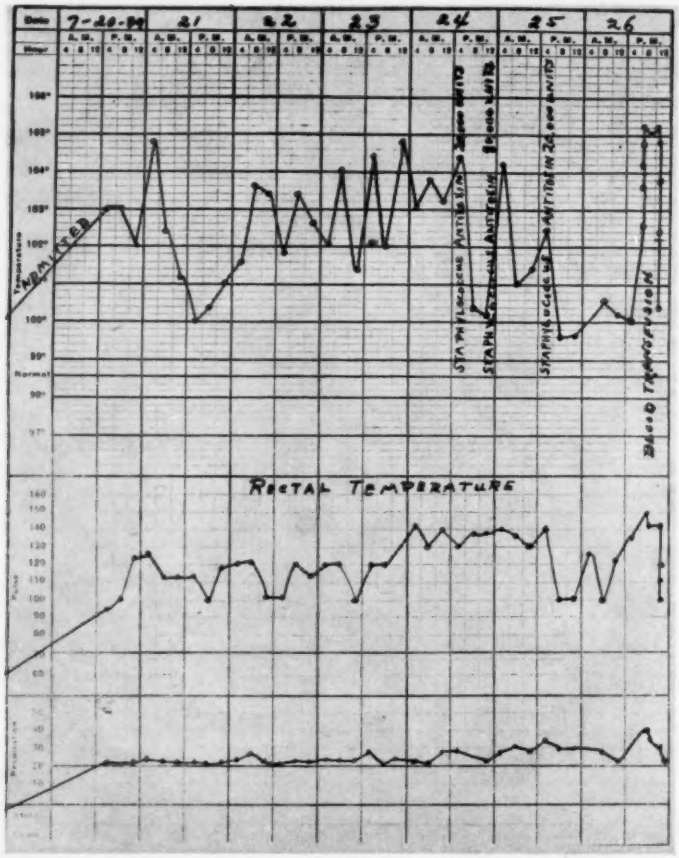

Fig. 2.—The effect of staphylococcus antitoxin on a child 4 years old with a hemolytic *Staphylococcus aureus* septicemia.

It has been suggested that staphylococcal antitoxin acts in the following ways: "The toxin produced by the staphylococcus in vivo is neutralized by this antitoxin; a component of the immune serum may act on the staphylococci and increase the ease with which they are phagocytosed by certain organs, especially the liver and spleen. The antitoxin in the circulation may also inhibit the action of leucocidin and thus allow the polymorphonuclear leucocytes to phagocytose the bacteria in either the blood or the tissue."[4] If staphylococcus antitoxin acts in this manner, then it may help indirectly in phagocytosis, a process most important in eliminating bacteria from the body.

CHEMOTHERAPY

There is the problem of the effects produced by staphylococci per se on the tissues of the body in addition to the action of the toxin. Some cultures of staphylococci do not produce toxin in vitro, and furthermore, should the toxin be neutralized in vivo, the bacteria remain. The result of the many experiments on phagocytosis, opsonins, agglutinins, increased rate of removal of staphylococci from the blood stream of immune animals, and the "microbic tissue-affinity" have not solved the problem of the morbidity and mortality of staphylococcal infections.

There was some expectation that the problem of the treatment of staphylococcal infections would be solved following the introduction of sulfanilamide. There have been many observations, both experimental and clinical, discussing chemotherapy.[27-42] Farrell,[43] in discussing these experimental observations, says, "Only a broad hint as to therapeutic efficiency is gained from these experimental studies."

A knowledge of the action of sulfanilamide and its associated compounds on staphylococcal toxin is important since it has been established both experimentally and clinically that staphylococcal toxin is a factor to be considered in many of the staphylococcal infections. Carpenter and his associates[44, 45] found that the lethal action of staphylococcal toxin for mice was inhibited when the toxin was mixed with sulfanilamide preceding an intraperitoneal injection but Rigdon and Avery, in unpublished experiments, found that the hemolytic and the skin necrotizing action of staphylococcus toxin was not inhibited by either sulfanilamide or sulfapyridine. Rigdon and Freeman[46] concluded from their studies that "the hemolytic, the skin necrotizing and the lethal factors in staphylococcus toxin apparently are not affected by sulfapyridine." Baylis[47] observed that the addition of various dilutions of sulfanilamide, sulfapyridine, and sulfathiazole to a dose of staphylococcus toxin slightly enhances rather than neutralizes the lethal action of the toxin. Furthermore, he has shown that the dermonecrotic toxin, the coagulase, and the enterotoxin are not neutralized by solutions of the sulfanilamide tested at 37.0° C. The experimental results of Baylis,[47] and Rigdon and Freeman,[46] would suggest that sulfanilamide and its derivatives effect staphylococci, probably by inhibiting the growth and the multiplication of the organism, thereby indirectly decreasing the production of toxin and not by directly neutralizing any of the toxic substances produced by the bacteria.

The methyl and phenyl thiazole derivatives of sulfanilamide are markedly bacteriostatic for *Staph. aureus*.[48] In this connection, Rigdon and Freeman[46] observed that sulfapyridine in extract broth has a bacteriostatic effect upon staphylococci. In these experiments there was observed a considerable variation in the action of this drug upon the different strains of staphylococcus. The strain most susceptible to the

action of sulfapyridine was a nontoxic-producing organism. In contrast to this, the two strains of staphylococci most resistant to this drug were both toxin-producing organisms. It will be necessary to make subsequent studies to determine whether there is any correlation between the toxin production and the bacteriostatic resistance of staphylococci to sulfapyridine.[46]

Chemotherapeutic agents now are used almost routinely in the treatment of staphylococcal infections. The clinical results obtained with the different preparations vary. Sulfathiazole, however, appears to be of greater value than sulfanilamide and sulfapyridine in the treatment of staphylococcal infections. An editorial[49] appearing in the *Lancet* in August, 1940, discussed this problem. It stated that "for staphylococcal septicemia the new sulfathiazole (M & B 760) is recommended (12 to 15 gr. daily). . . . Much has been expected of the sulphonamides and much has been attained, but many patients with staphylococcal . . . septicemia still die despite the new chemotherapy and if progress is to be made our failures as well as our successes should be recorded."

The clinical results following the use of sulfathiazole frequently have been very good. Alya and Roberts[50] reported cures in six cases of staphylococcal infection in the urinary tract. Helmholz and Larson[51] found sulfathiazole bactericidal for the staphylococci in the urinary tract. A concentration of 300 mg. per 100 c.c. was suggested for the treatment of urinary tract infections.[51] Staphylococcal infections in the meninges also have been successfully treated with sulfathiazole.[52, 53]

Sulfathiazole has been applied locally in the treatment of certain staphylococcal infections. The preparations used have included sulfathiazole crystals, an aqueous suspension of sulfathiazole used as an irrigant and also for saturating dressings, and sulfathiazole suspended in cod-liver oil. The success of the local use of sulfathiazole, according to Spink and Paine,[54] is dependent in a great measure upon maintaining a lesion free of purulent and necrotic material. According to these investigators the clinical results obtained so far warrant further investigation of this form of therapy.

The opinion, as expressed by Spink and Paine following the local application of sulfathiazole, apparently may also be made about all the published results of the chemotherapeutic agents used in the treatment of staphylococcal infections. The data at this time apparently are insufficient to evaluate the efficiency of these chemotherapeutic agents; however, in view of the fact that they may be given to patients with only a little likelihood of unfavorable results, it appears to us that their use should be continued.

A COMBINATION OF CHEMOTHERAPY AND SEROTHERAPY

The use of two therapeutic agents simultaneously may not be considered always advisable. Such a combination, however, has been used

in the treatment of pneumococcal infections. Long and Haviland[55] in discussing the problem of pneumonia with reference to chemo- and serotherapy say, "Patients who are severely ill should receive specific serum in addition to either sulfathiazole or sulfapyridine." De and Basu,[56] in 1938, first suggested that a combination of serum and a chemotherapeutic agent may offer advantages in staphylococcal therapy. Approximately a year later an editorial in the *Lancet*[57] suggested that "combined chemo- and serotherapy would seem to deserve an extended trial." In August, 1940, a second editorial[49] in the *Lancet* stated that in septicemia and bacteremia "antisera have gone out of fashion but the antitoxins to both *Staphylococcus aureus* and *Streptococcus pyogenes* should be used in full doses along with chemotherapy in any fulminating septicemia due to these organisms. The sulfonamides have their greatest sphere of usefulness in the prophylaxis of septicemia by localizing an infection already established in the tissues or by preventing infection where there is a strong likelihood of its occurrence." As recent as October, 1940, Farrell[58] expressed the opinion that "a few unreported clinical trials of combined treatment with antitoxin and sulfapyridine have been strikingly successful." Experimental observations on mice support these clinical observations.[43, 56, 58]

Goldberg and Bloomenthal,[59] in April, 1941, reported a series of thirty-two cases of staphylococcal septicemia in which various types of therapy are used. These investigators conclude that "of the various types of therapy employed in any one series, staphylococcus antitoxin and sulfapyridine gave the most direct evidence of favorably influencing the course of the disease." The following case is one included in the paper by Goldberg and Bloomenthal and illustrates the use of chemo- and serotherapy in the treatment of acute staphylococcal septicemia.*

Case Report (No. 30).—A 10-year-old male had a small carbuncle on his neck for one week prior to his admission to the hospital on Feb. 12, 1939. His temperature was 102.8° F. and the family was told that the fever seemed out of proportion to the size and appearance of the lesion. That afternoon, under ethylene anesthesia, crucial incisions were made and frank pus was evacuated. Cultures of this pus revealed a *Staph. aureus*. In the next twelve hours the patient had three chills and the temperature rose to 104° F. The boy was very toxic; he vomited several times and was irrational at intervals. His leucocyte count was only 6,900. It was thought that he had a fulminating septicemia, probably staphylococci. Blood was drawn for culture and vigorous treatment was instituted. He was given 30 gr. (2 Gm.) of sulfapyridine by rectum every four hours. He received 250 c.c. of blood by indirect transfusion, following which a total of 110,000 units of staphylococcus antitoxin was administered intravenously. The antitoxin was diluted by saline solution and it was given over a period of eight hours. Fifteen minims of adrenalin solution (1:1,000) were given with this foreign serum since the patient was allergic. His temperature reached 106.6° F. that night. It then dropped rapidly to normal and remained there except for a slight transient rise which occurred two days later.

*Permission to include this case and Fig. 3 is granted by Goldberg and Bloomenthal.[59]

At this time *Staph. aureus* in pure culture was reported as grown from the blood. Soon after the antitoxin was given the vomiting stopped. This permitted the oral administration of 60 gr. (4 Gm.) of sulfapyridine in divided doses to be given daily for the next two days. It was then stopped because of the rapidly improving general condition. The blood sulfapyridine level was 5.1 mg. per 100 c.c. three days following hospitalization. An urticaria developed on the seventh day and remained until the eleventh day. A daughter furuncle occurred in the neck and was drained; with these exceptions the patient's convalescence was uneventful.

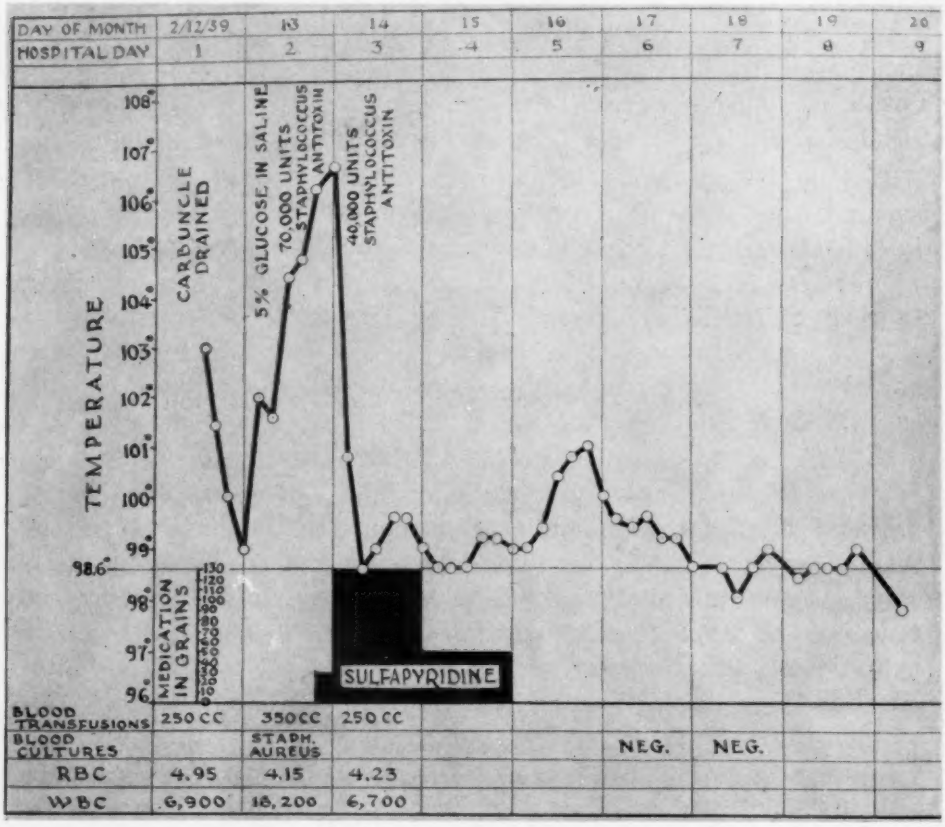

Fig. 3.—The effect of a combination of sulfapyridine and staphylococcus antitoxin on a child ten years of age with a *Staphylococcus aureus* septicemia.

BACTERIOPHAGE

This form of therapy has been advocated for the treatment of a variety of bacterial infections. Staphylococcal infections are included in the group. There have been many cases of dermitis, furunculosis, and septicemia treated with phage. In considering the efficiency of this form of therapy Longacre[60] says, "the evidence is equivocal and in many instances indicates that bacteriophage treatment in these lesions has no advantage over other forms of specific therapy." The potency of phage is important and some investigators think that this factor alone accounts for the disrepute into which phage therapy has fallen.

The mode of action of staphylococcal bacteriophage is not as obvious as that of staphylococcal antitoxin. Phage is neither a toxin nor an antitoxin.[61] However, Longacre has suggested that the evidence indicates that part of its therapeutic action may depend upon its antigenic properties.[60]

The mortality in cases of acute staphylococcal septicemia treated with phage is surprisingly low as shown by the following data: seven cases treated with one death, a mortality rate of 14.2 per cent.[62] Longacre,[60] and Jern and Meleney[63] report a mortality of 28.5 per cent in a group of twenty-one cases and 73 per cent in a second group of fifteen cases. These authors emphasize, however, the greater potency of the phage used in the treatment of the former group. McNeal and Frisbee report[64] a mortality of 75 per cent in a group of 100 cases of staphylococcal septicemia treated by the intravenous injection of bacteriophage.

There is some evidence to indicate that phage may increase the leucocytic response of experimental animals to the staphylococcus and probably increase phagocytosis. Until the mechanism of the action of staphylococcus bacteriophage is better understood and the clinical evidence of its efficiency is unequivocal it appears to us at this time that certain therapeutic agents other than phage may prove more efficacious in the treatment of staphylococcus septicemia.

STAPHYLOCOCCUS TOXOID

The treatment of recurrent staphylococcal infections of the skin is frequently a difficult problem. Since the staphylococcus may serve as an antigen it would seem that a person with a recurrent staphylococcal infection should have a higher immune titer than normal individuals. One must remember, however, that the production of immunity is not dependent on the antigen alone but also on the reactivity of the host.

Experimental and clinical observations have been made with both viable and heat-killed staphylococci.[65-69] There is a diversity of opinion as to the clinical value of vaccines in the treatment of staphylococcal infections. Klotz and Holman[70] state that the use of vaccines with killed staphylococci has a long and variable history of great successes and failures.

Burnet,[71] in 1929, was the first to prepare a staphylococcal antigen by detoxifying a staphylococcal filtrate with formaldehyde. This and similarly treated preparations have been studied extensively both experimentally and clinically.[72-75] The Council on Pharmacy and Chemistry accepted staphylococcus toxoid in 1935.[76]

Whitby,[77] in 1934, treated a group of 100 patients who had localized staphylococcal infections with staphylococcal toxoid and found that it gives more consistent results than any other antigen. He emphasized the fact, however, that patients vary in their response to staphylococcus toxoid. Whitby,[78] in 1936, again reported his results on a larger series

of patients treated with toxoid and concludes at this time that "Staphylococcal toxoid injected intramuscularly is a safe antigen giving rise to a relatively small number of minor reactions. Staphylococcal toxoid gives a good clinical result in a high proportion of cases of recurrent and resistant furunculosis, and is useful in the treatment of styes and carbuncles. It is not effective in pustular acne and sycosis with the dose employed in this series."

DISCUSSION

It appears at the present time that any rational approach to the problem of therapy in staphylococcal infections is difficult. This no doubt results from the wide variation in the action of different strains of staphylococci and also in our inability to satisfactorily classify them as of the pathogenic and the nonpathogenic strains. The coagulase test may be the most satisfactory method at present for the separation of the pathogenic and nonpathogenic organisms; however, the division into hemolytic and nonhemolytic strains is very important. The rapidity in which the latter division can be made is valuable from a clinical standpoint. The hemolysis as observed on blood agar media in which rabbit red cells are used occurs earlier and forms a larger zone than with any other known type of blood agar medium.

Staphylococcus antitoxin that neutralizes the hemolytic factor in staphylococcus toxin also will neutralize the so-called skin necrotizing factor, the nephrotoxin, and the acute killing factors.

The role that staphylococcus toxin may play in certain staphylococcal infections has been discussed. Antitoxin apparently is the only therapeutic agent that will neutralize the toxin and thus eliminate its action upon the tissues. Antitoxin is indicated in those cases in which there are the clinical manifestations of a toxemia. It is of questionable value, however, in cases of localized staphylococcal infection such as chronic osteomyelitis and carbuncles. It is not indicated in cases of recurrent furunculosis. The antitoxin should be given early in the disease and in large quantities. The dose should be an amount sufficient to produce an excess of antitoxin in the circulating blood. The minimum dose should be 100,000 units preferably given intravenously. In severe infections with profound toxemia 300,000 to 400,000 units of antitoxin may be required. This foreign protein is rapidly eliminated from the body and is usually absent from the blood in five to seven days. Parrish's technique may be used to demonstrate antitoxin in the blood.[26] The appearance of natural or spontaneous antitoxin in the blood in the absence of irreparable damage to important viscera is in our opinion a favorable sign.

Certain of the sulfanilamide derivatives are bacteriostatic and in the presence of sulfanilamide an increase in phagocytosis in vitro has been observed. Information at this time is meager as to the strains of staphy-

lococci that are susceptible to these drugs. Certain experimental observations indicate that none of these drugs, however, have any effect upon the toxins produced by some strains of staphylococci. Sulfanilamide, sulfapyridine, and sulfathiazole have little if any therapeutic value in the treatment of staphylococcal infections. The newer chemotherapeutic agents have been used for an insufficient period to satisfactorily evaluate them from a therapeutic standpoint.

It would seem that a combination of staphylococcal antitoxin and either sulfapyridine or sulfathiazole is the most satisfactory form of therapy, especially for those cases of severe staphylococcal infections in which the patient presents signs of a toxemia. This combination is most important if the staphylococcus is hemolytic. The antitoxin will neutralize any toxin that has not united with the tissue cells. As far as we know, neither antitoxin nor any chemotherapeutic agents will have any effect on the tissues injured by both the bacteria and the toxin previous to the administration of the drugs. The sulfanilamide derivatives may act directly or indirectly on the bacteria and thereby diminish the formation of toxin. The need for continuing the use of antitoxin will be determined by the individual case. The maximum effects from the antitoxin when used in combination with a chemotherapeutic agent will occur within the first few days of the disease.

Chemotherapy and serotherapy in staphylococcal infections cannot replace surgery. To drain a localized lesion is to eliminate a potential focus for the formation of toxin and the point from which bacteria may enter the circulating blood. Supportive measures are always indicated, such as transfusions for the anemia. The albumin-globulin ration in the blood should be retained, as should the sugar and the chloride levels. From the immunologic standpoint one must always remember that active immunity to staphylococcal infections develops slowly and the period of its efficiency is not known. On the other hand, passive immunity manifests its action immediately and its effect persists for only a few days.

CONCLUSION

One important way in which staphylococci may effect the host is through the effect of its toxin on the parenchymatous tissues. The exotoxin produced by the staphylococcus may be neutralized by specific antitoxin. It is necessary to give the antitoxin before the toxin becomes fixed to the tissues. Toxin apparently is present in over 90 per cent of the cases of staphylococcal septicemia. It is capable of producing death or it may be only of secondary importance in the pathologic processes.

The action of the chemotherapeutic agents apparently depends upon their inhibitory influence on bacterial growth. They do not neutralize staphylococcal toxin. It is difficult to accurately determine at this time their clinical efficiency.

A combination of chemotherapy and serotherapy may offer the best results in the treatment of staphylococcal septicemia. The efficiency of any form of treatment, of course, is in direct ratio to the duration of the infection, the toxin producing ability of the organism, and the resistance of the host. The earlier any treatment is begun the better will be the therapeutic response.

Chemotherapy and serotherapy are only adjuncts to surgery. They should not be considered as agents to replace it in the treatment of localized staphylococcal infections.

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Editorial

The Delayed Classification of Burns

CERTAIN techniques of medical thought, originally contributions of value, may, although they have outlived their usefulness, become so ingrained in the literature that they remain to becloud rather than illuminate the subject. In this class may be placed, perhaps, the commonly accepted American classification of burns into three "degrees."

Within obvious limits, the surface area governs the mortality of a burn and the depth, the morbidity. The purpose of measurement of extent is to afford prognostic data as to survival; the purpose of measurement of depth, that is, "degree," is to afford prognostic data as to the time of healing and the necessity for skin grafting. The only useful classification of depth would be one to give that information.

"First degree" and "second degree" burns, of course, present no problem of depth. There is no marked loss of tissue and, hence, little epithelial growth is initiated. Even the severest of them needs only the replacement of incompletely destroyed surface epithelium. If infection is excluded and the burned area is not large enough to cause death, such burns are always well within a few days.

If we examine, however, the severest degree permitted by the traditional classification we find a different state of affairs. By definition, a "third degree" burn means a burn that is deep enough to entail loss of substance, but it does not define the depth of loss. And in that deficiency resides its lack of usefulness as a description of prognostic significance.

To appreciate the truth of this statement, one need only consider the processes of healing at various depths of burning. If destruction includes the entire dermis, then epithelization must proceed from the edges only; if it includes only a part of the skin depth, then healing will occur throughout the burned area from thousands of minute epithelial elements, the remaining fragments of papillae, hair follicles, and glands. In the former instance spontaneous healing accompanied by scar contracture is a matter of months, if it ever occurs, and even a relatively satisfactory result depends upon skin grafting. In the latter instance, however, if infection and chemical abuse are avoided, one cannot prevent healing, a process usually complete within three weeks and accompanied by no contracture of scar. And yet these two diverse pictures are included under a single classification.

The reason for the tenacity of a poor term is not too hard to understand. The depth of a burn in relation to full or partial thickness of

the skin cannot be judged on inspection when first seen. The history may allow a guess as to probabilities. The high-temperature, short-duration burn (for example, from a gasoline explosion without ignition of the clothing) is more apt to be superficial than the low-temperature, long-duration burn (for example, the scald from more than momentary immersion in water close to 100° C.), yet on superficial inspection the appearances of the two may not differ. Even were a biopsy permissible, it might not yield the desired information since the deep limits of many burns cross and recross the critical level, leaving islands of preserved gland epithelium scattered throughout an expanse of complete thickness destruction. In other words, the diagnosis of the one thing important in prognosis as to morbidity is impossible at the time many burns are first seen. Only examination after sloughing has occurred will furnish the desired information. What is needed in classifying burns is the general recognition of this fact.

A classification may be suggested in which this limitation is accepted. A simplification of Dupuytren's classification is proposed, dividing all burns into three groups, which will be separately defined and discussed below. In order to make a sharp departure from traditional thought, the use of the word "group" is suggested rather than "degree." The classification is based almost entirely upon the therapeutic problems involved.

The proposed classification is as follows:

Group I. This is the most superficial type of burn and includes all burns now classified as "first and second degree." The reason for combining the two under one head is that there is little difference in treatment and none in prognosis. In many instances the diagnosis of a Group I burn can be made on first inspection.

Group II. All burns involving loss of substance in which the loss nowhere includes the full thickness of the skin. This group requires protection from damage and contamination, takes somewhat longer to heal than Group I, but does not require skin grafting for a satisfactory result. It cannot be diagnosed until after sloughing has occurred.

Group III. This burn includes the full thickness of the skin and any structures beneath. It requires skin grafting for a satisfactory result. It also cannot be diagnosed until removal of the slough. Many, if not most, of Group III burns will present peripheral or central areas of Group I and Group II destruction. This latter fact is of no practical significance since these areas will declare themselves before skin grafting can be undertaken.

Group III corresponds to the fourth and higher degrees of Dupuytren's classification. It is interesting that the value of Dupuytren's grouping has not been recognized in American thought. Perhaps impatience to offer an immediate prognosis is the explanation. Certainly

the general acceptance of Dupuytren's classification would adequately fulfill the purpose of the present proposal.

The observers who are studying burns during the present acute interest in them, are, of course, well aware of the importance of the critical level between Groups II and III. The majority of readers of the ever-growing literature may not be thinking in these terms. To them all "third degree" burns may be the same and may offer the same problems and the same prognosis; this fogginess of thought will continue as long as the authorities continue to present two distinct conditions under one heading. It may be that the present lack of unanimity of opinion on the proper local therapy for burned surfaces has arisen because of the failure to discriminate between degrees within the "third degree." Certainly the literature is full of photographs of so-called response to specific types of therapy in individual burns that would obviously heal promptly under any nondestructive regime. A recent striking moving picture of a theoretically sound method of therapy shows just such a burn. The less experienced might believe that all "third degree" burns will heal in a manner equally dramatic and prompt.

If a more rational classification yields dependable evidence in guiding local therapy, the gain will outweigh the disadvantage entailed by delayed classification in the individual case. There is no point in attempting to measure the depth of a burn before it is possible to do so.

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

LIVER CHANGES IN HYPERTHYROIDISM

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INTRODUCTION

IN VIEW of the intense and varied metabolic activity of the liver, it would seem reasonable to assume that this organ especially would feel the increased drive of hyperthyroidism and in the recent literature increasing emphasis has been placed on the clinical importance of the liver changes occurring during this disease. Evidence of these changes is given by jaundice,[9, 46, 65] which not infrequently occurs in association with the more severe forms of thyrotoxicosis, by other disturbances of liver function measurable by various laboratory tests,[7, 46, 49, 61, 70] and by liver lesions often found at autopsy in those dying of the disease.[9, 12, 65, 69] Whether the injury is due to the effect of increased amounts of the thyroid hormone on the liver cells, or to the injurious action of some other substance or factor on a liver made vulnerable by the functional strain of hyperthyroidism, is a moot point.[54] The weight of evidence in the opinion of the reviewer seems to favor the latter theory. In any case, damage to the liver must be taken into consideration in the clinical management of a case of hyperthyroidism, particularly when the added stress of anesthesia and operation must be faced. It would seem, therefore, that an evaluation of the problem and a consideration of the possible available therapeutic measures to minimize or prevent the hazard of liver injury associated with hyperthyroidism might prove useful.

POST-MORTEM DATA

Liver lesions in wide variety have been found at autopsy in patients dying of hyperthyroidism, and have been reported in the literature by various authors.

Beaver and Pemberton[9] in their analysis of 107 autopsies on patients dying with exophthalmic goiter noted two outstanding types of hepatic change, acute and chronic. The acute changes they described as fatty metamorphosis and central or focal necrosis. These authors pointed

out that while such lesions occur also in various conditions other than hyperthyroidism, they were encountered so consistently in their series of autopsies (in all but 9 of the 107 cases, or 91 per cent) that it was felt impossible to ignore them as a characteristic feature of the disease. In five of their cases the lesions were so pronounced as to be comparable to those found in moderately severe acute yellow atrophy. Raab and Terplan[59] and Kerr and Rusk[40] also reported finding degenerative liver lesions in hyperthyroidism similar to those found in acute yellow atrophy.

Two types of chronic lesions, also, were described by Beaver and Pemberton. The first and most important of these was a condition which they designated "chronic atrophy," the term referring to the loss of weight of the liver.* This change was found in 66.55 per cent of the livers examined. It was frequently associated with the acute degenerative changes described above, and at times with some degree of cirrhosis. In many instances when the acute degenerative lesions were not present, no histologic change was found in these atrophic livers. In some instances, however, the liver cells were small and at times there was some increase in the connective tissue, which in certain cases was limited to the hepatic tissue near Glisson's capsule.

The second chronic lesion described by these authors was cirrhosis, present in about 60 per cent of their series, and apparently a late stage of the acute and atrophic changes described above. The microscopic changes found in association with the cirrhosis they considered similar to the "chronic parenchymatous interlobular hepatitis" described by Weller.[69]

Weller, in 1933, studied forty-eight autopsies performed on patients dying with exophthalmic goiter and contrasted the liver lesions with those found in an equal number of carefully selected autopsies on patients dying from other causes. This author found various degenerative lesions in the livers of patients dying of Graves' disease, such as cloudy swelling, fatty infiltration, and pigment atrophy. These he considered might be due to the direct effect of thyrotoxicosis; but he pointed out, as did Beaver and Pemberton,[9] that this cannot be proved, since such lesions are frequently encountered also in autopsies on patients dying from other causes. One type of lesion, however, he considered specifically associated with Graves' disease, and described as a "patchy, chronic, parenchymatous, interlobular hepatitis," involving the peripheral portion of the lobules to a moderate degree and showing more fibrosis and lymphatic infiltration than bile duct proliferation. He found chronic hepatitis in forty-two of the forty-eight autopsies on patients dying with Graves' disease, while in the control series it was found in but fifteen instances, being well marked in only one.

*It is interesting that hyperthyroidism in animals produces hypertrophy of the liver; possibly the end stage of this would be atrophy.

Cirrhosis of the liver in association with exophthalmic goiter has also been reported by Marine and Lenhart,[50] who state that this condition has been observed in a significant number of long-standing cases coming to autopsy. These authors noted that the connective tissue increase varied from a slight thickening of the portal spaces to well-marked, fibrous bands, while the liver cells themselves usually showed some fatty changes. Goodpasture,[26] in reporting autopsies on two patients dying of exophthalmic goiter, stated that the liver in one case was definitely cirrhotic and in the other showed central congestion, moderate fatty changes, and numerous vacuolated nuclei. Widespread pathologic changes consisting of congestion, fatty infiltration and degeneration, necrosis, inflammation, and connective tissue proliferation were noted by Habán[29] in the livers of patients dying of exophthalmic goiter. He considered that these lesions were caused by the toxic action of the disease and to denote their specific nature he proposed the term "cirrhosis basedoweana," or "hepar basedowanum."

Cameron and Karunaratne,[12] in a study based on autopsies of 40 cases of proved exophthalmic goiter, classified the liver changes in 4 groups: first, passive venous congestion, of which there were 10 cases; second, fatty changes with or without necrosis, of which there were 5 cases; third, atrophy and nodular formation, likewise 5 cases; and, fourth, cirrhosis, 10 cases. In summary, they found that 2 out of 3 cases showed liver changes independent of passive venous congestion and they considered it possible to distinguish between cases in which passive venous congestion resulting from cardiac failure was primarily responsible for the pathologic changes and those in which the changes occurred independently of stasis, agreeing in this with Habán. Fatty changes occurred frequently and they attached little significance to this finding unless associated with definite necrosis, in which event they regarded the condition as evidence of toxemia and probably the basis for the chronic findings that they described as atrophy and cirrhosis.

Boyce and McFetridge,[10] found liver changes at autopsy in six cases where the patient had died in a thyroid crisis. The lesions were classified as "fatty infiltration or degenerative changes ranging from mild changes to actual necrosis, cirrhotic changes, and acute yellow atrophy." The authors further stated that, "frequently the same liver revealed various degrees of all changes in different areas and as a rule there was a significant decrease in weight."

Another series of autopsies upon patients dying with hyperthyroidism was analyzed by Shaffer[65] from the Cincinnati General Hospital. This author found a high incidence of hepatic lesions, more than one type of lesion being present in the majority of the livers examined. The change that he considered of greatest significance was a chronic interstitial hepatitis, sometimes associated with cirrhosis. These lesions were not considered to be the result of chronic passive congestion, as was the cen-

tral necrosis of the liver lobules that he observed at times. Fatty changes occurred so frequently and were of such severity that this author felt they must be taken into account, although he pointed out, as have others before him, that they occur also in many conditions other than hyperthyroidism. In regard to cirrhosis, he found this lesion in 25 per cent of his autopsies on patients dying of hyperthyroidism, while in a control series the incidence was only 4.7 per cent. Shaffer further noted that the occurrence of cirrhosis did not appear to depend on deficiencies of vitamins A and C.

Lord and Andrus[48] carried out various studies on 680 patients with hyperthyroidism who had been subjected to some type of operation on the thyroid gland during the previous eight years. Sixteen of these patients had died, eight of them in typical thyroid crisis. Six of the sixteen were autopsied and the pathologic changes found in the liver were said to resemble those described by Beaver and Pemberton.[9]

In summary, numerous studies have been carried out on autopsy material from patients dying of hyperthyroidism, and the frequent occurrence of liver changes, both acute and chronic, has been reported. The acute lesions varied from minor fatty changes to degeneration so severe that it was comparable to that found in acute yellow atrophy. The chronic changes consisted of hepatitis, cirrhosis, and atrophy, and at times both acute and chronic lesions were found in the same liver.

Two series of autopsy studies on hyperthyroid patients have been reported by Means,[54] and Lewis,[45] who did not find the liver lesions impressive. Means, in commenting on the liver changes reported by other authors, as described above, considered that these lesions were probably a complication of thyrotoxicosis rather than an integral part of the disease. He believes it likely that the liver under conditions of hyperthyroidism is particularly vulnerable to various types of injury, possibly due to its depletion of liver glycogen or to other causes.

CLINICAL EVIDENCE

Jaundice.—In addition to post-mortem data pointing to liver damage in association with hyperthyroidism, we have clinical evidence in jaundice, which occurs as an occasional complication of this disease.

Case reports of jaundice occurring in hyperthyroidism have for a long time appeared in the literature at infrequent intervals. In 1874, Habershon[30] reported such a case in which the jaundiced patient was a young woman, 20 years of age, suffering from exophthalmic goiter complicated by rheumatic fever. At autopsy the pericardium was found to be acutely inflamed and covered with "shaggy membrane"; but there was no apparent liver lesion. Sutcliff and Durh,[68] in 1898, reported "an extraordinarily acute case of Graves' disease" in which slight jaundice developed. The patient died three months after the first symptoms; there was no autopsy. In 1906, Eder[21] reported three

cases of jaundice occurring in patients with exophthalmic goiter. All three patients recovered from the jaundice; one passed gallstones.

The causes of jaundice are obviously numerous; and some of the early case reports are open to criticism both because the jaundice may have occurred from some pathologic process entirely unrelated to the thyroid and also because the diagnosis of hyperthyroidism may have been inaccurate. With the added evidence, however, of later reports of the clinical and pathologic data in a relatively large number of cases of hyperthyroidism, it has become evident that while jaundice is not common in this condition it is by no means rare in the more severe cases. In 1919, Kohn[41] analyzed a series of 56 cases of exophthalmic goiter and reported the occurrence of jaundice in five. Heilmeyer,[35] in 1931, reported that among 101 cases of exophthalmic goiter, 6 patients showed jaundice that could not be explained on any other basis. Weller,[69] in 1933, reported jaundice in 8 of 35 patients whose cases he analyzed. Beaver and Pemberton,[9] also in 1933, reported the occurrence of this complication in 23 (21.5 per cent) of their series of 107 cases of exophthalmic goiter, pointing out, however, that the jaundice was slight in 17 instances and pronounced in only 6. In Shaffer's[65] group of 24 thyrotoxic patients,* studied in 1940, jaundice was present in 5 and well marked in 3. Lichtman,[46] in 1941, reported that among 26 cases of Graves' disease autopsied at Mount Sinai, jaundice occurred twice. Kerr and Rusk[40] reported the clinical and pathologic findings in a patient operated upon for hyperthyroidism from which he had suffered for about 3 months. He ran a rather stormy postoperative course during which he developed jaundice which gradually became deeper, death occurring 15 days after operation. On autopsy the liver showed almost complete loss of architecture with necrosis and cellular infiltration.

Liver Function Tests.—Various laboratory tests have been used to elicit further information as to possible alterations of liver function during hyperthyroidism.

Blood bilirubin in the presence of hyperthyroidism has been measured in the belief that increased amounts of this pigment in the blood stream, in the absence of excessive hemolysis of red cells or of obstruction of the excretory ducts, would indicate impaired function of the liver parenchyma. Youmans and Warfield[70] carried out this test in twelve cases and found increased bilirubin in seven. Maddock and collaborators[49] also reported finding hyperbilirubinemia in certain of their hyperthyroid patients.

Various dyes have been used to determine the functional efficiency of the liver in hyperthyroidism. Youmans and Warfield,[70] using the

*Three of the 24 patients were admitted in thyroid crisis and of these, 2 were jaundiced.

Rosenthal modification of the phenoltetrachlorphthalein test, found that twenty-two of their forty-four hyperthyroid patients showed evidence of liver injury. The bromsulfalein test, used by Maddock and associates,[49] indicated impaired liver function in eight of thirteen patients (or 61 per cent).

Glucose, galactose, and levulose tolerance tests have also been used to provide an indication of liver function in the presence of hyperthyroidism. Youmans and Warfield,[70] working with glucose, found that nearly all their cases showed some abnormality in the characteristic curve of the blood sugar concentration, but were unable to correlate these abnormalities with the indications of liver damage afforded by the phenoltetrachlorphthalein test. Althausen and Wever[4] reported that the curve of galactose in the blood after oral administration was considerably elevated in patients with hyperthyroidism. They believed this might be accounted for by impaired utilization of galactose by the liver, or possibly by accelerated intestinal absorption. Lichtman[46] also carried out galactose tolerance tests on thirteen patients with hyperthyroidism, in seven of whom he found a normal galactose excretion, while in six pathologic galactosurias were encountered. This author further noted a definite tendency for galactose tolerance to improve during the course of iodine therapy. Levulose tolerance tests were used by Youmans and Warfield,[70] who concluded that this method was definitely inferior to the phenoltetrachlorphthalein test in detecting impaired liver function.

It is questionable how much significance should be attached to any of the various sugar tolerance tests as pointing to specific injury to the liver in hyperthyroidism, for it must be borne in mind that complex disturbances of carbohydrate metabolism are present in this condition, and also that the rate of sugar absorption from the alimentary tract is probably increased.[4]

Approaching the study of liver function during hyperthyroidism from another point of view, Maddock and co-workers[49] studied the blood amino acid nitrogen in these patients. No abnormal values were found; but this is not surprising, since the deaminizing function of the liver is lost only in the presence of extensive liver damage, such, for example, as occurs in the terminal stages of acute yellow atrophy.*

Cinchophen oxidation in cases of uncomplicated hyperthyroidism was studied by Lichtman[47] who found that disturbances of this process existed in sixteen of his twenty cases (or 80 per cent), indicating moderate impairment of liver function. Severe damage to the liver, however, was in no instance indicated.

*It should be noted that liver damage as severe as that found in acute yellow atrophy has been reported occasionally in patients with marked hyperthyroidism (Kerr and Rusk.)[40] Presumably, in these patients the blood amino acid nitrogen would show abnormal values.

Recently, several investigations of liver function in hyperthyroidism have been carried out by using the Quick hippuric acid test, which is based on the assumption that the liver is involved in the conjugation of benzoic acid and glycine to form hippuric acid. Bartels[7] found that reduction in liver function was shown by this test to exist in a high proportion of hyperthyroid patients, only 18 out of the 148 such patients giving a normal response at the time of admission to the hospital. The degree of impairment of liver function appeared to be in direct proportion to the severity of the hyperthyroidism. In cases of primary hyperthyroidism, improvement occurred during preoperative treatment; no change, however, was apparent in cases of adenomatous goiter with hyperthyroidism. Boyce and McFetridge[10] and Haines and associates[32] have also reported finding disturbances of liver function in hyperthyroid patients by use of the hippuric acid test. Haines and his co-workers go on to say, however, that since the reduction of hippuric acid excretion is not uniformly found in patients who are considered by other standards to be poor surgical risks, they do not consider this test to be of great value in the clinical management of patients with hyperthyroidism.

A different method of testing liver function was used in 1941 by Lord and Andrus.[48] These authors had previously found that patients with intrahepatic jaundice had reduced values of plasma prothrombin, and that on injection of 2-methyl-l, 4-naphthoquinone, the plasma prothrombin content did not rise significantly. In cases of extrahepatic jaundice, on the other hand, the plasma prothrombin did rise significantly following injection of this drug. These authors, therefore, suggested that the response of a low level of plasma prothrombin to the injection of 2-methyl-1, 4-naphthoquinone might be considered a measure of hepatic function. With this in mind they studied the level of plasma prothrombin in a series of thirty-six hyperthyroid patients and found that whereas the preoperative level of plasma prothrombin showed no direct correlation with the severity of the hyperthyroidism, a significant fall took place postoperatively in twenty-nine out of the thirty-six cases of toxic goiter and furthermore, that the extent of the fall could be closely correlated with the severity of the postoperative course. Apparently, however, these authors did not test the response of the patients to the injections of the 2-methyl-1, 4-naphthoquinone.

EFFECT OF THYROID CRISIS ON THE LIVER

Although the frequency of the thyroid crisis and postoperative storm has been greatly reduced by the introduction of iodine therapy, these reactions have by no means disappeared* and probably account for over half the number of deaths resulting from thyrotoxicosis.[8, 23, 49] Since patients developing these reactions suffer from the most severe

*Pemberton[38] points out that some reaction occurs after every operation for active exophthalmic goiter, although the typical severe reaction is no longer common.

form of hyperthyroidism, it is not surprising that the various manifestations of depressed liver function, including jaundice and degenerative liver changes in those coming to autopsy, have frequently been found in such cases.[10, 17, 49] Indeed, the theory has been advanced that the changes taking place in the liver are themselves responsible for the occurrence of the thyroid crisis,[10] and a similarity has been seen between certain clinical features of the crisis, especially hyperpyrexia, and the syndrome that accompanies the so-called "liver deaths."[10, 11, 44] Exception to this view is taken by Maddock and his co-workers,[49] who could find no correlation between the preoperative determination of hepatic function and the mildness or severity of the reactions following operations on the thyroid gland. These authors further point out that while an increase in the symptoms of hyperthyroidism together with a measurable decrease in liver function often occur postoperatively, they found nothing to show that one was the cause of the other. While to me also, the evidence seems weak in favor of the theory that the primary pathology responsible for the crisis is to be found in the liver, injury to the liver does undoubtedly occur frequently as a complication of the crisis, often playing an important part in the clinical picture and even contributing to a fatal outcome.

DATA FROM ANIMAL EXPERIMENTS

There is little exact information on the interrelationship of the liver and the thyroid under normal conditions. A survey of the literature, however, brings out several points. Complex iodine products in general are eliminated by the liver, and it is believed that this also applies to the thyroid hormone, its destruction and excretion taking place by means of this organ.[1, 60] There is also some evidence that under certain conditions thyroxin may be stored in the liver.[2, 3, 71] Thus, Zavadovsky and Azimov[71] reported that after a large dose of thyroxin they were unable to find the hormone in the blood until after the lapse of four hours and they considered that during this interval the hormone was accumulating in the liver.

That certain changes are produced in the liver by experimental hyperthyroidism has been known for a long time.

Hypertrophy of the Liver.—As early as 1916, Hoskins[38] reported that in thyroid-fed albino rats the liver appeared considerably heavier than in the controls. In 1920, Hewitt[36] likewise reported a hypertrophy of the liver in thyroid-fed animals. In 1930, Simonds and Brandes[66] carried out an extensive study on dogs, in which body weights and liver weights were compared in normal, thyrotoxic, and starved animals. These authors found that whereas in starvation the liver lost weight in greater proportion than the body, in thyrotoxicosis the liver loss was less, proportionately, than that of the body as a whole. They point out that this is particularly striking since we know that glycogen is lost from

the liver in both starvation and hyperthyroidism, and that, consequently, something must occur in this organ to counterbalance the loss of liver weight which one would expect from the loss of liver glycogen in the thyrotoxic animals. These authors are inclined to the view that the relative, if not absolute, hypertrophy of the liver during experimental hyperthyroidism is caused by the increased and augmented blood flow to this organ.*

In 1933, Higgins[37] confirmed the finding that feeding thyroid extract to rats tended to produce an increase in the size of the liver. He further showed that when a subtotal removal of the liver was carried out, the rats receiving thyroid regenerated their liver tissue more rapidly than animals similarly operated upon but receiving no thyroid.

Change in Liver Glycogen.—Perhaps the most widely recognized effect produced in the liver by the increased thyroid hormone in the blood is a marked decrease in liver glycogen.† This important finding was first reported in 1913, by Cramer and Krause,[15] and has since been confirmed by many other workers. Cramer and Krause carried out their work on cats and rats and reported that after small amounts of fresh thyroid gland had been administered for two or three days to these animals, even though they were on a carbohydrate-rich diet, the liver was found to contain only a trace of glycogen. They believed that this was due to an inhibition of the glycogenic function of the liver and not to an increased utilization of carbohydrates.

The above findings of Cramer and Krause were confirmed in 1917 and 1918, by Kuriyama,[42, 43] and in 1933, by Coggeshall and Greene,[13] who further reported that when thyroxin and desiccated thyroid gland were given in equi-iodine doses, the former preparation lowered the liver glycogen more than did the latter.

Drill[19] reported in 1937, that he was able to maintain a normal level of liver glycogen in thyroid-fed rats by administering large doses of the vitamin B complex.

Histologic Changes.—Histologic changes are said to occur in the liver when experimental hyperthyroidism is produced in animals. One of the earliest studies on this aspect was carried out in 1913, by Farrant,[22] who produced hyperthyroidism in cats and rabbits by feeding thyroid extract, and reported finding histologic changes in the liver, occurring most markedly in the center of the lobules. He described these changes as fatty degeneration.

In 1921, Hashimoto[34] produced hyperthyroidism in albino rats by feeding desiccated thyroid gland. This author was chiefly interested in the changes in the heart, but also reported finding pathologic changes in the liver both in animals dying during the course of the experiment

*The kidney and heart also show an increase in size.

†The phenomenon of decreased liver glycogen in hyperthyroidism is so constant that it has been suggested as a test for the presence of the thyroid hormone in unknown preparations (Dresel and Goldner).[18]

and in those sacrificed at an earlier stage in the experiments. The lesions varied from relatively simple fatty degeneration to actual necrosis. They were most marked around the central veins, but at times involved the entire lobule. In the periphery of the lobules showing degenerative changes, he frequently found evidence of reparative processes, as indicated by a large number of mitotic nuclei and young cells with clear protoplasm and large nuclei. In animals dying after a long course of thyroid administration, there was evidence of chronic passive congestion.

In 1933, Gerlei,[24] working with rabbits, studied the effect produced on the liver by administering large amounts of thyroxin. The animals were given daily subcutaneous injections of 4 mg. of thyroxin and death ensued in four to five days. In addition to finding hypertrophy of all the organs, he found extensive degeneration and necrosis of the liver resembling that found in chloroform poisoning. The necrosis was most marked around the central veins, and while the necrotic areas themselves showed very little fat, the boundary zone between the necrotic and normal cells showed large amounts.

Liver Function Tests.—There are very few reports on liver function tests during experimental hyperthyroidism in animals. Youmans and Warfield[70] reported some preliminary experiments in which liver function was determined by use of the phenoltetrachlorphthalein test. These workers found that thyroid-feeding of their animals had no effect on the functional efficiency of the liver as estimated by the above test. Drill and Hays[20] studied the liver function in hyperthyroid dogs by means of the bromsulfalein method. They found that after prolonged feedings of thyroid extract to these animals, disturbance of liver function usually developed and the dye retention was greatly increased by reducing the amount of yeast in the diet or omitting it entirely. These authors do not claim that deficiencies of the B vitamins were the only factors in diminished liver function in their hyperthyroid animals, but they feel that there was some causal relationship between disturbances of liver function and the insufficient intake of these vitamins.

INCREASED SUSCEPTIBILITY OF THE LIVER TO INJURY UNDER CONDITIONS OF HYPERTHYROIDISM

Increased Susceptibility to Chloroform.—It has already been suggested that the liver under conditions of hyperthyroidism may be more susceptible to injury by various agents than it is normally. In order to test this hypothesis, a number of attempts have been made to ascertain the effect of various well-known liver poisons during hyperthyroidism. One of the first of such experiments was carried out by Davis and Whipple,[16] who tried the effect of feeding thyroid to the experimental animals prior to the administration of chloroform by inhalation.

These authors concluded that the administration of thyroid had no influence on the liver injury following chloroform anesthesia,* and that the only notable finding in the liver at autopsy was the unusually small amount of fat. These experiments are open to certain criticisms, in that only four animals (dogs) were used, that they received thyroid treatment for only four days, and that the chloroform was given by inhalation only and not by injection. The significance of this latter point is brought out by Goodpasture,[25] who, in studying the effects of light chloroform anesthesia on the myocardium of hyperthyroid animals, noted that although the thyrotoxicosis did increase the susceptibility of the heart muscle to the toxic action of chloroform anesthesia, the livers of these animals usually showed no central necrosis. When, however, the chloroform (in small doses of 0.2 c.c. per kg.) was administered subcutaneously, the animals usually died within twenty-four hours with extensive liver necrosis. No control experiments were carried out to show the effect of chloroform injections on the livers of animals not receiving thyroxin.

McIver,[51] however, in 1940, showed that the administration of crystalline thyroxin to albino rats definitely increased their susceptibility to chloroform poisoning. The chloroform in these experiments was administered by subcutaneous injection, 0.4 to 1.5 c.c. per kg. of body weight, to animals that had received injections of crystalline thyroxin over a period of one to two weeks. Of fifteen animals (rats) so treated, eleven died in twelve to thirty-six hours, while four recovered. In the control group of twenty rats which received the chloroform injections but no preliminary treatment with thyroxin, all recovered or were sacrificed at the end of forty-eight hours, showing no symptoms of chloroform poisoning. In 1942, McIver and Winter,[52] in experiments on the mechanism of the increased susceptibility to chloroform poisoning found in hyperthyroid rats, showed that it could not be attributed simply to the fact that the liver glycogen is depleted by the administration of thyroxin. These authors further showed that the administration of a high protein diet did not protect the livers of the hyperthyroid rats from injury following chloroform injections.

Carbon Tetrachloride Experiments.—Cameron and Karunaratne,[12] in 1935, could not find that liver damage from toxic doses of carbon tetrachloride was increased by feeding thyroid extract to the rats.

Effects of Intercurrent Infection.—There is some evidence in the literature that the liver of hyperthyroid animals is particularly susceptible to intercurrent infection. Thus, Habán[28] found, in 1935, that the most extensive liver lesions in animals rendered toxic by the administration of thyroid preparations were in those where intercurrent infection oc-

*It is interesting that Davis and Whipple's[16] experiments were suggested by Hunt's[30] observation that the administration of thyroid preparations exercises a protective action against acetonitrile poisoning. As stated above, they concluded that it neither protected the liver against chloroform poisoning nor apparently increased the amount of damage done by the anesthetic.

curred.* In 1941, Sealy[64] found that when animals infected with Shope's papilloma were given thyroid extract, liver changes developed, whereas, such lesions were not found in two groups of controls, one of which was receiving thyroid extract without infection with Shope's papilloma, the other being infected with Shope's papilloma but receiving no thyroid preparation.

Deleterious Effects of Anoxia.—Recent experimental work[53] showed that when hyperthyroid animals were exposed to artificial atmospheres containing low percentages of oxygen, degenerative lesions could usually be demonstrated in the liver, varying from slight changes when the anoxia was of short duration, to extensive degeneration when the anoxia was of longer duration. The livers of normal animals similarly exposed to anoxia showed no liver lesions. The mortality among the hyperthyroid animals was high,† while there were no deaths among the controls.

Since anoxemia, due to a number of causes (respiratory obstruction following operation, pulmonary edema, hyperpyrexia), is commonly encountered in hyperthyroidism,[14, 31, 49, 62] particularly in relation to the thyroid crisis and postoperative storm, this condition may be an important etiologic factor in some of the instances where degenerative lesions are found at autopsy.

THERAPEUTIC IMPLICATIONS

Since the liver lesions associated with hyperthyroidism have been reported only in severe or long-standing cases, it is obvious that early recognition and efficient treatment of the underlying disease would largely do away with this complication. Neglected and fulminating cases of thyrotoxicosis, however, continue to be seen and it is worth while to consider what measures can be taken to protect the liver in such circumstances.

In the literature dealing with the general subject of liver injury, emphasis is laid on the protection afforded to the liver by certain elements of diet, notably proteins and carbohydrates.[16, 27, 55, 56, 57] But it should be noted that however convincing the evidence in favor of the protective effect of a high protein diet against liver poisons in general, hyperthyroidism produces a new set of conditions under which the protective action of proteins may not apply. This is true also of the protective value of a high carbohydrate diet or the intravenous administration of glucose, for it must be remembered that a serious derangement of carbohydrate metabolism occurs in hyperthyroidism and that the reduced ability to store glycogen in the liver is one of the

*Schultz,[63] in 1939, demonstrated that the myocardium of hyperthyroid animals showed lesions only when intercurrent infection was present. In these experiments, chronic, focal, hemolytic streptococcus infection was produced in hyperthyroid rabbits. Characteristic myocardial lesions were found at autopsy in these animals, whereas none were seen in the control animals. Schultz makes no reference to the liver.

†It has been known for some time that hyperthyroid animals tolerate anoxia poorly.[5, 6, 67]

outstanding features of the disease. It is possibly significant that in recent investigative work it was found that neither a high protein diet nor injections of glucose were effective in protecting the livers of hyperthyroid animals against chloroform poisoning.[52] The nutritional needs of the body, however, are enormously increased during hyperthyroidism and this fact alone, aside from any specific protective effect on the liver, is sufficient to warrant emphasis on the inclusion of adequate amounts of protein and carbohydrate in the diet of these patients.

The vitamin needs of the body are also greatly increased during hyperthyroidism and should be adequately met. That this is particularly true of the B vitamins, is suggested by Drill's work[19] in this field. As already pointed out, this author reported that the B vitamins are beneficial in maintaining a normal level of liver glycogen during experimental hyperthyroidism and in later studies with Hays[20] demonstrated that they are of assistance in maintaining a normal dye excretion.

Since the liver under conditions of hyperthyroidism shows increased susceptibility to injury, and it is uncertain how much protection is afforded by measures that would be effective under ordinary conditions, special precautions must be taken to guard this organ from exposure to deleterious factors. In view of what has been said as to the apparent influence of intercurrent infections upon the development of liver lesions in hyperthyroidism, especial care must be taken to shield the patient from any infection. Other deleterious factors assume particular importance when an operation is to be carried out. An anesthetic should be selected that has a minimum toxic action on the liver and the greatest care should be used to see that no anoxemia results either during or subsequent to administration. In the more fulminating cases of hyperthyroidism the use of local rather than general anesthesia should receive careful consideration. During the postoperative period, if any evidence of anoxemia develops due to respiratory obstructions or pulmonary complications, prompt oxygen therapy should be instituted. It should also be remembered, as pointed out by Hartman,[33] that hyperpyrexia in itself may contribute to anoxia and the beneficial effect of oxygen therapy in the thyroid crisis, where hyperpyrexia is such a constant feature, is well recognized.[31, 62]

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Review of Recent Meetings

MEETING OF THE AMERICAN SURGICAL ASSOCIATION, APRIL 6-8, 1942, CLEVELAND, OHIO

J. DEWEY BISGARD, M.D., OMAHA, NEB.

ADDRESS of the President, Harvey B. Stone, Baltimore.—Homeostasis demands constant defense against (1) trauma, (2) parasites, (3) psychic and emotional influences (in man), and it also demands the maintenance of body economy. Cancer represents an escape from normal restraints, a breakdown of homeostasis. The mechanisms of defense are (1) encysting, (2) suppurative, (3) immune bodies, and (4) antiphylactic reaction. Cross grafting in higher forms of life is defeated by host defense reaction. The graft is already adapted to the habitat from which it is removed and unable to adapt itself to its host which reacts against it. The fundamental factor may be the genes which determine specificity, or simply the reaction to protein molecules. Grafting or replacement surgery is an enormous unexplored field. It is within the realm of possibility in the future to transplant from one individual to another not only vital organs but even extremities. For successful transplanting of tissue such as thyroid it is necessary to (1) use small transplants, (2) obtain complete hemostasis and use strict aseptic and atraumatic technique, (3) be assured of good blood supply in the recipient bed, (4) (?) physiologic need of transplant, (5) (?) placement of graft into its natural region.

The Control of Hair and Feather Pigmentation as Revealed by Grafting Melanophores in the Embryo, B. H. Willer (by invitation), Chicago.—All pigment cells for the skin, hair, and feathers migrate in the embryo from the neurocrest cells. Transplants from the neurocrest of pigmented breeds of chick embryos, such as black leghorns, to the site of the wing bud of embryos of nonpigmented breeds, such as white leghorns, caused these latter chicks to grow a wing with black feathers and vice versa. These transplanted melanophores are affected by such hormones as estrin, thyroid extract, and desoxycorticosterone. These substances profoundly influenced the color of the feathers. Melanophores from the white breeds produce no color because they die early; this explains the graying of hair in man. Premature graying represents premature death of melanophores, either on a familial or a hormonal basis.

Studies in the Free Transplantation of Skin, James Barrett Brown, St. Louis.—Epithelization of donor sites of split skin grafts has been found to occur within six days with new squamous epithelium "dedifferentiating" from the remnants of follicles deep in the derma. If the healing stimulus is low, epithelization of any defect in the skin is retarded. Fibroplasia is also retarded so that there is less contracture. When large burned defects heal by "scar" epithelium there are fissuring and breaks in the epithelium with excitation of the healing stimulus over a long period of time which may result in malignant degeneration. The progression of this benign proliferative activity of the epithelium to a malignant invasive one was demonstrated.

Homografts have been observed to survive in identical twins. Under other circumstances they persist for a few weeks and then are lost. Their use as emergency dressings for burns was demonstrated. They were used simply to cover the surfaces until they were replaced by the patient's own epithelium.

Clinical and Experimental Studies in the Treatment of Burns, Vinton E. Siler (by invitation), and **Mont R. Reid,** Cincinnati.—Evidence from both clinical and animal studies was presented that compression dressings over burned surfaces reduces the loss of plasma from those surfaces, thereby conserving plasma and diminishing thermal shock. These dressings are applied after the surfaces have been meticulously cleansed with rigid aseptic technique and then covered with vaselineized gauze. The burned areas are put at rest and the extremities splinted or encased in plaster of Paris. Subsequent dressings were done infrequently. Often second-degree burns were healed at first redressment. In 145 cases so treated there were five deaths and in these five over 40 per cent of the skin surface was burned.

In the discussion, **W. G. Penfield,** Montreal, stated that the care of burns was the biggest problem of the War in Britain. **S. L. Koch,** Chicago, reported 480 cases of burns with 3.9 per cent mortality using the technique of cleansing with copious washing with saline solution, débridement, vaseline gauze dressings with compression, immobilization in splints, and adequate plasma and other shock therapy. He believes that this method with slight modification could be used in military surgery. **L. Elloeser,** San Francisco, and **E. Young,** Rochester, N. Y., reported experiences with and recommended immediate excision of areas burned to third degree and covering these areas with split grafts immediately. With takes the areas are covered with skin within a few days and infection and contractures avoided.

Chronic Infected Burns With Hemorrhage, William A. Altemeier (by invitation), and **B. N. Carter,** Cincinnati.—In three cases in which bleeding had persisted in spite of all forms of treatment, the oozing stopped promptly and permanently following applications of zinc peroxide. From only one of these cases however were anaerobes cultured.

In the discussion, **F. L. Meleney,** New York, stated that anemia in infected burn cases resulted from hemolytic activity as well as capillary bleeding, and that symbiotic infections including anaerobes were prone to cause capillary oozing.

Procurement and Use of Blood Substitutes in the Army, Douglas B. Kendrick, Jr., Major, M.C., U.S.A. (by invitation).—The Red Cross operates eighteen blood donor stations throughout the country where blood is taken from 1,500 volunteers daily. For the service, plasma is packaged in both dry and wet forms. There is available over 250,000 units of dried plasma. From its use there have been only .2 per cent reactions and none severe. Recently, the albumin fraction has been extracted from plasma and packaged in 25 per cent solutions in smaller bulk to fascilitate storage and shipping. Fifty cubic centimeters have an osmotic pull of 250 c.c. of plasma.

The Problem of Intestinal Gases Complicating Abdominal Surgery, Albert O. Singleton, Galveston.—A study of intestinal gases shows that they are composed mainly of swallowed air. Experimental evidence was given which indicated that distention of the intestine seriously modifies its normal function, resulting in disturbance of electrolytic balance in the blood, as well as seriously interfering with the circulation of the bowel. A clinical study of gastric suction as compared to duodenal suction indicates that in the former there is very little fluid lost, while in the latter there is a great deal of fluid lost. Postoperative ileus is of little consequence in the absence of distention; the return of peristalsis following abdominal operations is much more prompt if gases are not allowed to enter the intestine; the loss of fluids and electrolytes by gastric suction is small in amount and can be easily replaced by parenteral methods; one of the greatest adjuncts to abdominal surgery for the comfort of the patient and the lowering of mortality is the use of gastric suction to prevent intestinal distention.

Since air is swallowed during induction of anesthesia the stomach should be intubed and aspirated before and during operation.

In the discussion, **W. D. Gatch,** Indianapolis, reminded the group that distention causes atelectasis and anoxia by elevating the diaphragm and limiting its excursion. **A. O. Whipple,** New York, stated that ileus may be caused by edema of the bowel resulting from hypoproteinemia and overhydration. Intestinal intubation is desirable in conjunction with resection of the right colon. **F. A. Coller,** Ann Arbor, stated that much air is swallowed during the excitement stage of anesthesia. **W. G. Maddock,** Ann Arbor, believes that much air may enter the stomach without being swallowed.

Small Intestinal Distention: A Study of Five Years' Treatment, Charles G. Johnston, and **R. J. Noer** (by invitation), Detroit.—This study of a series of cases with small bowel distention showed that decompression with suction applied through a tube indwelling the stomach, duodenum, or (particularly) the small bowel down to the level of the obstruction is an invaluable aid as an adjunct to other methods of treating intestinal distention and obstruction. It was curative alone in some cases. Its use, however, demands greater accuracy of diagnosis, particularly in respect to recognition of strangulation. It facilitates operation and postoperative care. Immediate or early operation should be done in every case in which the possibility of strangulation cannot be excluded.

New Operative Techniques in the Management of Bowel Obstruction, Owen H. Wangensteen, Minneapolis.—A definite, general lowering of the mortality of obstruction came about largely through development of nonoperative decompressive measures. Further reduction of the mortality awaits development of improved methods of dealing with the obstructed bowel surgically, by employment of primary resection and closed anastomosis in nonviable intestinal strangulations, and development of operative means of decompressing the distended bowel aseptically.

The intestine is perforated with a trocar containing a catheter fitted to a suction system. The bowel is emptied without soiling by pleating it over the catheter.

In the discussion, **L. S. McKittrick,** Boston, stated that nonoperative decompression has caused disastrous delay in certain cases and that immediate operation is indicated in all cases in which strangulation cannot be excluded. **Dr. Wangensteen,** in closing, stated that rebound tenderness was indicative of strangulation.

Experiences With the Surgical Management of Diverticulitis of the Sigmoid, R. H. Smithwick, Boston.—An analysis was made of sixty cases operated upon for diverticulitis and associated complications including acute perforation, localized abscess, vesicosigmoidal fistula, and external fistula, as well as subacute and chronic nonperforated lesions. The sigmoid was resected in thirty cases, employing four different techniques. Included with other methods of treatment were simple drainage and temporary colostomy. The mortality from resection was low and the ultimate results in the resected group were superior to those of the group treated more conservatively.

In the discussion, **H. W. Cave,** New York, stated a preference for radical resection and this by the exteriorization or Mikulicz type of operation. He stressed the frequency with which these lesions are explored and even resected upon a diagnosis of carcinoma.

Surgical Treatment of Malignant Lesions of the Sigmoid With Extension, Ralph F. Bowers, New York.—Four cases in which carcinoma of the sigmoid had infiltrated the bladder and in which the involved portions of the bladder had been resected along with the sigmoid were reported. In one case the entire bladder, prostate, and seminal vesicles were removed after transplanting the ureters to the colon. In this series the results of long cures have justified the radical nature of the operations.

In the discussion, **V. C. David,** Chicago, reported six personal cases in which portions of the bladder were excised and long periods of "cure" obtained. **R. B. Cattell,** Boston, stated that a preliminary transverse colostomy should be done and resection or drainage delayed. **R. K. Gilchrist,** Chicago, stated that studies of several resected specimens had failed to show carcinomatous infiltration of the bladder but rather that the fixation and fistulas were inflammatory.

The Operative Repair of Massive Rectal Prolapse, Roscoe R. Graham, Toronto.—Inasmuch as rectal prolapse is in reality a sliding hernia of the pouch of Douglas it should be treated as a hernia, applying the principles utilized in the repair of hernias elsewhere. An operation was described following these principles, namely, dissection and disposal of the sac, the extended peritoneal lining of the pouch of Douglas, and closure of the defect in the supporting levator ani muscles. Three cases so treated with good results were reported.

The Effect of Pneumonectomy Upon Cardiac Pulmonary Function in Adults, Andre Cournand (by invitation), and **Frank B. Berry,** New York.—From a study of pulmonary efficiency of the remaining lung and of cardiac efficiency following pneumonectomy in twelve cases, it was found that distention of emphysema of the remaining lung did not increase its efficiency but rather decreased it. Prevention or reduction of overdistention by means of thoracoplasty following pneumonectomy increased the efficiency as measured by methods of evaluating ventilatory function, efficiency of gas exchange, and cardian reserve. In a few cases dyspnea persisting many months after pneumonectomy was relieved following thoracoplasty.

In the discussion, **E. A. Graham,** St. Louis, stated that he had followed pneumonectomy by thoracoplasty in his earlier cases believing it necessary to help obliterate the empty cavity. Reinhoff's observations led him to abandon the procedure. He questioned the advisability of increasing the magnitude of the operation by immediately supplementing a thoracoplasty. In closing, Dr. Berry stated that they had found studies of oxygen saturation of the blood very helpful in determining the cause of dyspnea.

A Practical Consideration of Open Pneumothorax Under Sodium Evipal, Sodium Pentothal, and Ether Anesthesia, C. A. Moyer, J. B. McKittrick (by invitation), and **Frederick A. Coller,** Ann Arbor.—Under evipal and pentothal anesthesia dogs with induced pneumothorax developed expiratory predominance which persisted after termination of the pneumothorax. In two animals artificial respiration failed to re-establish normal breathing.

The predominance of expiratory activity instituted by open pneumothorax during moderate evipal and pentothal anesthesia has not been seen during moderate ether anesthesia. This finding coupled with the observation that hypercarbia and anoxia increase the toxicity of evipal and pentothal indicates that ether is superior to evipal and pentothal for anesthetizing persons suffering from penetrating wounds of the chest.

Clinical and Experimental Observations on the Closure of the Bronchus Following Total Pneumonectomy, William F. Reinhoff, Jr., James Gannon, Jr. (by invitation), and **Irwin Sherman,** Baltimore.—Leakage from the bronchial stump constitutes one of the major hazards following pneumonectomy. An extensive experimental study in animals and observations made in sixty-one cases subjected to pneumonectomy have indicated that the bronchial stump is most securely closed by placing two rows of interrupted sutures, the proximal one to relieve tension without strangulation and the distal row to accomplish approximation. Silk sutures are preferable. Much added security is gained by covering the stump with an adjacent flap or pedicle flap of pleura. In the sixty-one cases the bronchus opened in sixteen, or 26 per cent, and this caused death in three.

In the discussion, **E. A. Graham,** St. Louis, stated that he had sutured free, as well as pedicle, grafts of pleura over the stump. **N. S. Shenstone,** Toronto, demonstrated a method of closure of the stump in which the bronchus was crushed and ligated proximal to the suture line. **A. Ochsner,** New Orleans, stated that in a series of thirty-two pneumonectomies the bronchial stump opened in three and in two of these x-ray therapy had been given preoperatively.

Transthoracic Resection of Tumors of the Esophagus and Stomach, Edward D. Churchill, and **Richard H. Sweet** (by invitation), Boston.—In a series of twenty-one cases of carcinoma of the mid-portion of the esophagus, nine were resectable and of these, three survived and are living and well. They were resected by a modified Torek operation. An equal series of carcinomas of the distal one-third of the esophagus and cardia of the stomach were presented. In 23 per cent there were metastatic glands below the diaphragm along the lesser curvature indicating necessity of preliminary laparotomy. Resection was accomplished through a left thoracotomy wound. Since the esophagus has no serosa, accurate approximation of the mucosa in the anastomosis is essential.

In the discussion, **D. B. Phemister,** Chicago, reported twelve cases, with eight immediate survivors. There were seven of the lower third and cardia, with three survivors. **A. Ochsner,** New Orleans, stated a preference for the two-stage operation dividing the gastrohepatic omentum through the preliminary laparotomy wound and prefers the right thoracotomy approach for resection. It is important to anchor the stomach when it is drawn up through the incised diaphragm.

The Use of Oxygen in the Treatment of Transudation and Exudation Into the Lungs, Cecil K. Drinker (by invitation), Boston.—The lungs have rich lymphatic systems which drain into the right innominate vein. In presence of anoxia there is increased flow of lymph from the lungs and an increased permeability of the capillaries. Obstructed and forced breathing increases the flow of lymph and with anoxia, lymph exudes into the alveoli and interstitial spaces. This coating of lymph prevents air from reaching the capillaries and makes resuscitation impossible. Early recognition of disturbance of lymphatic flow and prevention of its exudation by prompt relief of obstructed and forced breathing and the administration of oxygen must be done before the irreversible stage is reached.

The Treatment of Metastatic Cancer of the Prostate, Charles Huggins, Chicago.—In many instances cancer of the prostate is very sensitive to hormonal changes. Castration in thirty-one out of forty-five cases caused moderate to complete regression of the neoplasm, including both local and metastatic lesions. Stilbestrol and x-radiation of the testes also cause regression, whereas testosterone causes an increase in the growth of the tumor, and in pain and other symptoms.

The prostate normally contains acid phosphatase. This is much increased with carcinoma as is the blood acid phosphatase. An increase of acid phosphatase of the blood is diagnostic of carcinoma of the prostate. Just as castration and stilbestrol cause regression of the neoplasm they decrease the blood acid phosphatase, and, conversely, testosterone increases it.

Cases with extensive bony metastases were presented showing amazing temporary cures with relief of all symptoms and disappearance of all evidence of the neoplasm following castration.

Reflexes Originating in the Common Duct Giving Rise to Pain Simulating Angina Pectoris, I. S. Ravdin, and **H. P. Royster** (by invitation), Philadelphia.—Pseudo-angina can arise from lesions in the common bile duct. The attacks of pain, while classical of angina pectoris, are prone to come on at rest in bed at night and are not associated with an effort syndrome. They may present electrocardiographic evidence of coronary disease which disappears as do the symptoms after surgical relief of the lesion of the common duct. Stimuli arising in the common

duct cause, in these cases, reflex spasm of the coronary arteries. There may or may not be intrinsic coronary disease with the superimposed spasm.

In two cases relieved of anginoid pain by removal of stones from the common bile duct the authors were able to elicit the same pain after operation by distending the common bile duct by injections through the T tube.

In the discussion, **C. G. Mixter,** Boston, reported three cases relieved of residual postcholecystectomy colic following lower dorsal sympathectomy. **G. J. Heuer,** New York, presented statistical data showing that there is a higher incidence of hypertension and cardiorenal disease in people with gall bladder disease than in those of the same age without this disease. **J. A. Wolfer,** Chicago, cited a case with the reverse situation, that is, coronary thrombosis with symptoms of gall bladder colic and a normal gall bladder. He also presented a case with a diaphragmatic hernia which gave rise to symptoms and electrocardiographic evidence of coronary disease.

Tests of Hepatic and Pancreatic Function in the Differential Diagnosis and Preparation of Patients With Lesions of the Biliary Tract, William D. Andrus (by invitation), **Jere W. Lord, Jr.,** and **Michael Lake,** New York.—The level and the response toward normal in prothrombin time to the parenteral administration of vitamin K is a guide to the functional status of the liver. By an analysis of the duodenal contents for the presence or absence and character of pancreatic ferments it is possible to determine the presence or absence of a concomitant obstruction of the pancreatic duct in jaundiced patients. Yeast contains a factor which aids in protection and regeneration of the liver as do carbohydrates, proteins, and choline. Avoidance of anoxia, which is very deleterious to the liver, is important.

In the discussion, **I. S. Ravdin,** Philadelphia, stated the simple truth that tissues can be built in regeneration only from proteins. Carbohydrates are essential to this process but aid only as protein-sparing substances. The best proteins for purposes of regeneration are the proteins of the liver itself. Cystine does give some protection to the liver.

Vitallium Tubes in Biliary Surgery, Herman E. Pearse, Rochester, N. Y.—In construction of bile ducts it is very desirable to preserve the sphincter of Oddi and so prevent regurgitation from the duodenum. Vitallium tubes for permanent bridging of defects in the common and hepatic ducts were demonstrated. These included a variety of design such as Y tubes to meet the various circumstances which might be encountered and a small tube for repair of chronic pancreatic fistulas. A few illustrative cases with very satisfactory results were presented.

In the discussion, **H. M. Clute,** Boston, reported one case with a satisfactory result. **E. W. Rockey,** Portland, reported satisfactory results in experimental animals with metallic magnesium tubes. **W. G. Maddock,** Ann Arbor, reported his experiences with the tubes in two cases, both unsatisfactory, followed by chills, fever, and icterus.

Carcinoma of the Pancreas and Ampullary Region, With Report of Six Additional Cases, Samuel C. Harvey, and **Ashley W. Oughterson,** New Haven.—Two cases were reported in which the body of the pancreas was resected for carcinoma, and two cases in which the head of the pancreas and the duodenum were resected for carcinoma.

In the discussion, **A. O. Whipple,** New York, reported a recently collected series of sixty-four cases of resection of the duodenum and head of pancreas. Of these, 35 per cent were done in one stage. Two cases followed over two years have shown no ill effect from loss of pancreatic juices; both can take 80 per cent of the normal amount of fat without digestive disturbance. **T. G. Orr,** Kansas City, and **V. C. Hunt,** Los Angeles, reported their experiences with four and five cases, respectively.

Spontaneous Internal Biliary Fistulae, Charles B. Puestow, Chicago.—An experience with sixteen cases with spontaneous internal biliary fistulae was reported. These fistulae communicated with the stomach, colon, duodenum, and choledochus. There was a mortality of 19 per cent in the series. From reflux and ascending infection, several cases had severe cholangitis. Icterus may be due to this factor or to obstruction. In most instances x-ray was diagnostic.

In the discussion, **H. H. Trout,** Roanoke, discussed the occurrence of obstruction of the bowel associated with fistulae, occasionally caused by large stones extruded into the gastrointestinal tract through the fistula. **J. M. T. Finney, Jr.,** Baltimore, reported two cases with multiple fistulae, one with fistulae between the gall bladder and stomach and duodenum and colon and the other between the gall bladder and colon in a case with actinomycosis. **J. D. Bisgard,** Omaha, reported a case of lymphosarcoma in which the barium given by mouth filled the common duct, thus leading to an erroneous diagnosis of fistula. By retraction the tumor had rendered the duodenal end of the common duct patulous so that barium passed into it from the duodenum. The duodenum in this case was resected by a one-stage Whipple operation.

Tissue Reaction to Ribbon Catgut and Preserved Ox Fascia Lata Strips, Amost R. Koontz, Baltimore.—Strips of ox fascia lata, if properly prepared, have certain advantages as suture material. They cause negligible reaction in the tissues and are not absorbed until replaced by fibroblasts which readily infiltrate them. They are also soft and pliable.

In the discussion, **D. B. Phemister,** Chicago, stated that tissue reaction to catgut resulted mainly from the fluid in which it was preserved. These chemicals should be soaked out. **J. A. Key,** St. Louis, found no foreign body reaction around ox fascia in experimental animals.

The Mechanism of the Action of X-ray Therapy Upon Infection, J. Dewey Bisgard, Howard B. Hunt (by invitation), **Orvis A. Neely,** and **Paul Scott,** Omaha.—Evidence that in rabbits x-radiation causes the liberation of a nonspecific antitoxic factor was presented. This factor was present in the peritoneal fluid and blood serum of these animals within twenty-four hours after irradiation, reached a peak of effective concentration in forty-eight hours, and was dissipated within seven days. This antitoxic substance caused survival of animals receiving a lethal dose of the toxins of both hemolytic *Escherichia coli* and diphtheria. When serum from irradiated animals was injected into normal stock animals a certain degree of passive immunity to these toxins resulted. This is at least in part an explanation of the beneficial effect of irradiation of infection.

In the discussion, **F. L. Meleney,** New York, stated that in addition to toxins, various chemical substances which are irritating to the tissues cause the development of nonspecific antibodies. **A. Brunschwig,** Chicago, in a study of cutaneous infections in a series of animals found that x-radiation reduced inflammatory reaction but did not prevent suppuration and necrosis or hasten resolution and healing.

Observations on the Loss of Nitrogen in the Immediate Postoperative Period, Alexander Brunschwig, Dwight E. Clark (by invitation), **and Nancy Corbin,** Chicago.—Results were reported of daily nitrogen balance studies during the first ten-day period following major operations in forty-one cases. As a result of protein catabolism there was a large negative balance (the loss of nitrogen in all excretions exceeding intake) in all cases save those in which the patients received proteins parenterally. The average daily loss in unsupported cases was 14 Gm. Several patients who received 100 c.c. of a 10 per cent solution of hydrolyzed casein daily were maintained in positive nitrogen balance much of the time. Some moderate transitory reactions occurred from the use of casein.

In the discussion, **Cox,** stated that amino acids regenerate plasma proteins equally well when administered by either oral or intravenous routes. **O. H. Wangensteen,** Minneapolis, said that surgeons must become more alert to the importance of nitrogen metabolism and the protein needs of surgical cases. The administration of amino acids causes little or no regeneration of plasma proteins because they are immediately utilized. **R. Elman,** St. Louis, stated that the colloidal property of amino acids was about the same as that of glucose and much less than that of plasma. In closing, **A. Brunschwig,** Chicago, stated that the use of amino acids was contraindicated in cases with damaged livers. Severe reactions occur in these cases. Casein can be given subcutaneously in 3 per cent solutions of distilled water.

The Nature and Functions of the Various Plasma Proteins and Other Possible Therapeutic Uses, Edwin J. Cohn (by invitation), Boston.—Plasma can be fractioned and the individual fractions utilized separately. The water-holding protein molecules of albumin exert approximately 80 per cent of the osmotic pull of whole plasma. Almost pure crystalline human albumin has been isolated and packaged in 25 per cent solutions for use of the armed forces. The albumin fraction of bovine plasma is almost identical to that of human plasma in its physiochemic properties and should be well tolerated by man. It is now undergoing clinical trial. As by-products of fractionations of the large quantity of plasma used in the study of human albumin, pure fibrinogen, thrombin, and prothrombin have been prepared and studied. When these fractions have been applied to oozing surfaces, bleeding has stopped almost instantaneously.

Observations on 1,000 Intravenous Injections of Hydrolyzed Casein in Postoperative Patients, Robert Elman, and **E. Bradley** (by invitation), St. Louis.—Out of 1,000 intravenous injections of hydrolyzed casein (Amigen*) to patients, postoperatively there were only two severe reactions (allergic). There were ten instances of chills and fever and incidence of phlebitis did not exceed that which occurs with glucose. Amigen was used in 2½ per cent and 5 per cent solution added to the glucose solution.

Recent Experiences in the Diagnosis and Treatment of Thrombophlebitis of the Lower Extremity, Jacob Fine, Boston.—When the occurrence of phlebitis of the femoral or iliac veins is obvious or suspected some corroborative evidence can be obtained by venography, and the site and extent of the thrombus determined. The associated spasm of the veins may simulate filling defects and lead to error in interpretation. Ligation and division of the femoral or iliac vein proximal to the thrombus prevents embolization and is indicated as a prophylactic procedure. The distal end of the vein is opened and the clot removed by aspiration. The femoral vein should be ligated proximal to the vena profunda. Several venograms demonstrating filling defects, spasm, etc., were shown and also cases in which emboli were showered repeatedly until ligation was performed above the thrombus.

In the discussion, **A. Ochsner,** New Orleans, reported ninety-one cases in which phlebitis had been promptly relieved and cured by novocain injection of the lumbar sympathetic ganglia. Only when embolization as evidenced by pulmonary infarction takes place is venography and ligation indicated and justifiable. **L. S. McKittrick,** Boston, stated that venography is inconclusive as to information and is a hazardous procedure. He favored high ligation in selected cases.

An Experimental Approach to the Problem of Menstrual Disorders, John C. Burch, and **Doris H. Phelps** (by invitation), Nashville.—Experimental studies were reported relative to the etiology of glandular cystic hyperplasia of the endometrium. Ovarian failure results from both intrinsic and extrinsic factors. It

*Mead Johnson & Co.

resulted from partial oophorectomy, partial thyroidectomy, and partial hypophysectomy. The male hormone caused repression while esterogenic substances caused regression.

In the discussion, **J. V. Meigs,** Boston, stated that tumors which produced the male sex hormone cause amenorrhea and that the endometrium which is under hormonal neurovascular control is influenced by many factors.

Vitamin Deficiency as a Factor in the Etiology of Surgical Diseases of the Digestive System, Frank K. Boland, Atlanta.—In countries where fresh foods form the chief diet, to the exclusion of foods preserved by canning and other methods, peptic ulcer, gall bladder disease, and appendicitis are almost unknown. Low incidence of these diseases exists among the Negroes of the South whose diet approaches that of primitive people. Among white people living in the same communities and eating sophisticated foods, these diseases are far more common. These facts may account in part for the rarity of ulcer, gall bladder disease, and appendicitis before the development of the art of preserving food. Artificial preservation of foods destroys or impairs their vitamin content. Surgeons should be concerned with the prevention of these diseases as well as their diagnosis and treatment.

In the discussion, **C. C. Lund,** Boston, stated that although some cases with peptic ulcers show deficiency of vitamin C, there is no consistent relationship and no clinical or experimental evidence in man to attribute ulcer to vitamin C deficiency.

Appendicitis in Infants and Children: A Fifteen-Year Review, Grover C. Penberthy, Clifford D. Benson (by invitation), and **Charles N. Weller,** Detroit.—In a series of 1,653 children under 12 years of age, with acute appendicitis, there were seventy-six deaths, an over-all mortality of 4.2 per cent. In the unruptured cases the mortality was 0.44 per cent, while in ninety-four cases with diffuse peritonitis it was 64.9 per cent. In cases with perforation and spreading peritonitis, nonoperative therapy including chemotherapy, parenteral fluids, and gastric siphonage was employed. Drainage was instituted early for all large abscesses and late for small ones. The type of incision did not influence mortality. The evidence was inconclusive relative to the controversy of immediate or delayed operation in cases with diffuse or spreading peritonitis. There was a lower mortality in the group of cases which received chemotherapy.

In the discussion, **W. C. Ladd,** Boston, reported 0.42 per cent mortality in his series of nonruptured cases and a reduction from 6 to 4 per cent in ruptured cases since the advent of chemotherapy. He condemned the indiscriminate practice of delaying operation. **F. A. Coller,** Ann Arbor, emphasized the importance of early operation in acute appendicitis by reporting a series of 2,700 cases of acute appendicitis in college students, with only three deaths. As a result of student health supervision these cases were operated early. **D. E. Robertson,** Toronto, reported 1,043 cases in children with only two deaths and stated his belief that death is usually caused by failure to control and relieve distention. **R. Elman,** St. Louis, stressed the importance of plasma and oxygen therapy for the very ill patients.

Closure of Ileostomy in Ulcerative Colitis, Richard B. Cattell, Boston.—The author proposed early ileostomy in patients with ulcerative colitis in order to obtain the earliest possible remission of the disease, before irreversible structural changes in the colon occur. The ileostomy may then be disconnected in some cases, restoring the continuity of the intestinal tract. Nine patients had closure of their ileostomies without operative mortality, five were successful, with no recurrence in two, and only temporary recurrence in three. The selection of cases for removal of the ileostomy is based upon: clinical remission maintained for one

year or more; healed process as observed by sigmoidoscopic examination; and distensibility, adequate lumen, and absence of obstruction, as determined by barium enema. If early ileostomy is elected for ulcerative colitis, the general mortality will be lower, complications will be reduced, and fewer permanent ileostomies will be necessary. Closure should be effected by suture of ileum to ileum.

Indications for ileostomy are (1) acute fulminating type of disease, (2) failure of medical management, (3) perforation, (4) hemorrhage, (5) obstruction, and (6) polypi.

In the discussion, **H. W. Cave,** New York, urged earlier use of ileostomy but cautioned that it should follow only after an adequate trial of medical treatment had failed. **W. E. Ladd,** Boston, reported three cases of ulcerative colitis in infants less than 6 months of age. Seven children in which ileostomies have been closed have remained well.

Skin Removal in Radical Mastectomy, William Crawford White, New York.—Follow-up observations of 254 cases that had had radical mastectomies for carcinoma five and more years previously showed that local recurrences and the mortality rate were not influenced by the extent to which the skin was excised. Many developed local recurrences but death resulted from distant metastases rather than local recurrences.

REPORT OF THE MEETING OF THE AMERICAN ORTHOPEDIC ASSOCIATION, BALTIMORE, MD., JUNE 3-6, 1942

GUY A. CALDWELL, M.D., NEW ORLEANS, LA.

THE members of the Association were guests of George Bennett and associates at Johns Hopkins Hospital, Wednesday, June 3, 1942. **Winthrop Phelps,** Baltimore, who has done a great deal of special work on spastic paralysis, demonstrated the diagnostic and prognostic value of injecting procaine hydrochloride into spastic muscles. A few cubic centimeters of procaine hydrochloride injected into the body of the paralyzed muscle will not only relieve the spasm but will permit normal activity of the opposing group of muscles. The surgeon can thus make a preoperative estimate of the extent of actual contracture and of the possibility of improved function in the opposing groups of muscles.

Kellogg Speed, Chicago, presented the history and slides of a patient who survived osteogenic sarcoma with numerous metastases in the lungs for approximately twenty years. Throughout this time the metastases gradually decreased in size without any particular treatment. The patient was subjected to numerous studies to ascertain, if possible, why the proved malignant tumors became stationary or regressed rather than advanced, but no satisfactory solution was found.

Henry Meyerding, Rochester, Minn., discussed spondylolisthesis. At the Mayo Clinic, between the years 1932 and 1938, there were 876 cases, 143 of which were operated upon. Analysis of the operative cases revealed that the results were excellent. The technique employed in the majority of cases consisted of exposure of the spinous processes, laminae and articular facets of the fourth and fifth lumbar vertebrae, and of the first three sacral segments. The articular facets were curetted, shavings reflected from the laminae, as in the Hibbs' procedure, and a double bone graft, taken from the tibia, was placed alongside the spinous processes which were not broken down. In addition, bone chips and shavings from the tibia were placed around the sides of the grafts to build up a rather massive lot of bone. Following operation, a simple dressing was applied and the patient allowed up with a reinforced canvas support at the end of three to six weeks.

Philip D. Wilson, New York, demonstrated a metal plate, properly shaped to fit the lumbosacral curve and adapted to internal fixation of the lumbosacral region. The plate extends from the spinous process of the fourth lumbar to the second sacral vertebrae and is fastened to each of them with a small bolt. After the plate is fixed in place, an osteoperiosteal graft from the tibia is placed over the denuded bone, as in other operations for spinal fusion. By this method of internal fixation the immediate postoperative pain is relieved, the period of bed treatment is shortened, the necessity for braces or fixation in plaster is eliminated, and earlier and more complete fusion is insured. Early results in twelve cases in which the operation was performed were excellent.

One of the highlights of the meeting was the visit of **J. A. MacFarlane,** Colonel, R.C.A.M.C., Surgical Consultant of the Canadian Active Service Force, who had been brought to this country by the Canadian government in compliance with the request of the President of the American Orthopedic Association to discuss the management of wounds encountered in modern warfare. He emphasized the importance of the immediate performance of surgical measures as the most effective means of preventing infection including gas gangrene. Chemotherapy was regarded as a valuable adjunct but he emphasized that it should not be substituted for surgical measures and could not compensate for incomplete débridement. He stressed the necessity for small, mobile, surgical units built into fast-moving trucks and so equipped that it is possible to operate within thirty to sixty minutes of arrival at a given post. The surgeons for such small units are necessarily young and strong but they must be competent in the surgery of trauma. MacFarlane approved the measures for the treatment of shock provided by the army at present in most places. He was of the opinion that the implantation of sulfonamides in the wound following débridement and repeated in subsequent dressings was probably a valuable adjunct to treatment only when adequate surgical measures were instituted early. He further emphasized the necessity of leaving all such wounds open. Infection, and particularly gas gangrene, had often resulted when attempts were made to close the wounds following débridement in the forward areas. He stated that when properly used the closed plaster method described by Trueta was proving satisfactory for most compound fractures. He advised, however, that in the case of fractures of the femur, in addition to the plaster, traction should be provided as soon as it could be adequately maintained. The use of toxoids in Canadian and British forces has proved most efficacious in the prevention of tetanus.

F. R. Hook, Captain, U.S.N., Washington, D. C., made an appeal to the assembled teachers and instructors in orthopedics in the various universities and hospitals throughout the country to make their teaching as practical and general as possible for the benefit of the men entering the army and navy medical services. He stated that particularly in the navy, men must be general surgeons and good physicians prepared to meet any emergency on board. In many instances, the working quarters on board are restricted, particularly when the ship is in action, and the treatment may have to be completed on the same ship. It appears that under existing conditions there is little opportunity for transfer of men and evacuation of the wounded. He suggested that the third- and fourth-year students should give actual treatment to the patients in the clinics and wards in order that they might be better able to perform their military duties. He felt that many of the special courses might safely be omitted in order to let the student do more practical work of the type he is likely to encounter in service.

Wallace Cole, Minneapolis, Minn., who has been serving at the American Hospital in England, presented moving pictures of "Pin Fixation in War Fractures." A number of compound fractures of the bones in the arms and legs have been treated by the two-pin method of Roger Anderson. The patients were permitted

to be ambulatory early in the treatment with good end results. He felt that the method is well adapted to a certain number of cases under suitable conditions.

Perrin Long, Baltimore, reviewed the subject of chemotherapy in the treatment of wounds. For local implantation, he advised sulfanilamide crystals of the size comparable to table salt. Sulfanilamide should be dusted over the surface of the wound; if the wound is to be closed, only light frosting of the drug is recommended. When wounds are to be left open, the drug should be sprinkled over the surface in such a way as to give the appearance of a heavy frost.

On Friday, June 5, an interesting symposium on the treatment of anterior poliomyelitis was given. Carefully analyzed end results were presented by various men to evaluate methods of treatment in various stages.

Arthur Steindler, Iowa City, discussed **Departures From the Principals of Absolute Fixation in the Treatment of Anterior Poliomyelitis** showing that absolute fixation of paralyzed extremities has many demonstrable disadvantages to both paralyzed and unparalyzed muscle.

Plato Schwartz, Rochester, N. Y., presented experimental evidence of spasticity of muscles in anterior poliomyelitis. Evidence of spasticity exists in muscles which apparently have never been affected as well as in the antagonists of the paralyzed groups. He further demonstrated relief of the spasticity after the use of hot packs over the affected muscles.

These presentations led to a discussion of the Kenny treatment in the early stage of poliomyelitis. The reports of various observers indicated that the treatment renders the patient much more comfortable, is probably most helpful in cases in which there is respiratory paralysis, and makes possible a program of early muscle training which is particularly helpful to those who are not so seriously paralyzed. It was pointed out by others, however, that some of the cases most publicized as having been actually cured were only slightly improved, as indicated by accurate muscle tests. In general, it is believed that the end results of this treatment are similar to the results obtained by the old methods of treatment. Most of the reports indicate, however, that the Kenny treatment, perhaps slightly modified, will probably be generally adopted for treating the acute stage of poliomyelitis. Patients, thus treated, will probably be more comfortable and will recuperate more rapidly but there will still be about the same proportion of cases with residual paralysis that require bracing and corrective operations.

LeRoy Abbott and associates of San Francisco, presented a moving picture demonstration of an operation for "Arthrodesis of the Wrist Joint." In it they emphasized the wide range of usefulness of this operation in paralytic conditions and arthritic processes involving the wrist joint.

Arthur G. Davis, Erie, Pa., discussed a small series of compound fractures of the extremities with large wound areas treated by careful débridement in the early hours, implantation of sulfanilamide, closure of the wound (even if skin grafts are necessary), and the application of pressure dressings similar to those used by the plastic surgeon in his routine skin grafting procedures. He demonstrated a number of forearm, hand, and leg fractures with excellent function following such treatment.

W. E. Gallie, Toronto, presented a group of fractures of the odontoid process, most of which had not been recognized until it was possible to use the laminagraph. Patients who suffered pain and in whom there was evidence of nonunion were successfully treated by the use of a bone graft and wire interposed between the spinous processes of the first and second cervical vertebrae. In these cases, the pain was relieved and a useful range of motion was retained.

Bruce Gill, Philadelphia, presented an end-result study, over a long period of years, of cases of congenital dislocation of the hip treated by him. This review is too valuable to be summarized; it should be carefully studied by everyone interested in this condition.

Carl Badgley, Ann Arbor, gave a brief review of a number of cases of spontaneous fracture of the neck of the femur following radiation for pelvic malignancy. He attributed most of these to the fractional method of treatment that was used in certain cases. It was interesting that most fractures united without difficulty but with some distortion and deformity unless they were nailed in proper position.

John Wilson and Francis McKeever, Los Angeles, reported a group of cases of osteomyelitis treated with sulfonamide drugs. The results were a distinct improvement over those of a former series of cases in which the drug was not used.

An unscheduled presentation was given by **Donald R. Webster,** Commander, Canadian Navy, on **Immersion Foot.** During the past year he has observed 142 victims who had been exposed in lifeboats or on rafts to cold water for a period of time varying from three days to three weeks. Prolonged immersion in cold water caused the feet to be cold, white, swollen, cyanotic in spots, numb, and lacking in tactile sensation. Rapid swelling, increased heat, and the appearance of blebs over the distal portion of the toes and sole of the foot resulted and was followed, in the severest cases, by gangrene. These patients were treated by refrigeration. When heat was used, gangrene with its tragic results developed. In the mild and moderately severe cases, within a period of from thirty to sixty days complete recovery was obtained by careful cleansing, application of ice bags over which insulating material was wrapped, and elevation of the extremity. The less severely injured patients suffered only some loss of tissue in one or more toes and the worst type of case required amputation.

J. A. Freiberg, Cincinnati, reported a series of approximately fifty cases of spinal fusion performed under a local anesthetic. He noted that this could be easily done, even in children. Some difficulty was encountered in obtaining grafts from the tibia because of pain arising from the endosteum. For this reason, a hole was drilled through the cortex into the marrow cavity at either end of the field from which the graft was to be taken. About 1 c.c. of procaine hydrochloride solution was then forced slowly into the marrow cavity at either end. Apparently, this sufficiently eliminated sensation from the endosteum to enable painless removal of the graft.

Fred M. Allen, New York (by invitation), presented a paper on **Refrigeration Anesthesia for War Injuries of the Extremities.** He reviewed the work that had been done at the City Hospital in New York in aged persons with diabetic and arteriosclerotic gangrene of the extremities. In these cases a tourniquet was applied at the proper level after the area had been desensitized by the application of ice bags. Morphine was administered, a tourniquet applied, and the extremity packed in ice up to and slightly above the level of the tourniquet. Amputation was then performed below the tourniquet, which was reapplied after the operation. Refrigeration of the extremity was continued for several days postoperatively during the healing period. It was gradually discontinued and the tourniquet finally removed. Excellent results were obtained. This technique was used in cases of compound fracture in which the vessels were so severely injured that amputation was necessary. It was proposed that ambulances and trains should be properly equipped with refrigerating units so that such injuries could be immediately frozen. This would enable transportation for an indefinite length of time without the risk of progress of infection or additional shock.

Book Reviews

A Textbook of Neuro-Anatomy. By Albert Kuntz, M.D. Ed. 3. Pp. 518, with 307 illustrations. Philadelphia, 1942, Lea and Febiger. $6.00.

This third edition, so completely revised that it is practically a new textbook, is one of a number of texts on neuro-anatomy which have been published recently. It is a well-balanced text for the elementary student. The figures are of the standard type without special features.

Each chapter, except the last or twenty-sixth, terminates in a summary which is brief yet sufficiently inclusive to be useful for review. The final chapter is a laboratory outline, thirty pages of which are devoted to this subject, and the final thirteen pages are clinical case reports, illustrating anatomic lesions.

Operative Surgery. By F. W. Bancroft, A.B., M.D., F.A.C.S., Associate Clinical Professor of Surgery, Columbia University, Ed. 1. Pp. 1102, with 250 illustrations, New York, 1941, D. Appleton-Century Company, Inc.

This volume, under the authorship of many well-known American surgeons writing upon subjects of their special interests, is an unusually good one. A note by the editor, F. W. Bancroft, suggests that this is the first of a number of volumes on operative surgery. The volume deals with general principles of surgical technique and abdominal surgery. There is a chapter on surgery of the esophagus and another on the mouth. The volume, therefore, deals essentially with the alimentary canal and its appendages and the peritoneum. In many ways, the book is a superior work and deserves to be in the hands of all who essay to do general surgery. The high light of the volume to the reviewer's way of thinking is the section on surgical manners and ethics written under the joint authorship of M. M. Stevenson and Mont R. Reid of Cincinnati.

Two of the sections in the monograph have appeared in larger monographs previously and the material here is, in a sense, the same in more concise form. There is some duplication in the effort throughout the book, which suggests a lack of editorial supervision. Three authors describe and depict operations for subphrenic abscess. A number of the illustrations fail to come up to the general standard of excellence expected of a work of this character. Indeed, it is not a little surprising that the editor did not exert his editorial prerogatives of demanding or seeing to it that only satisfactory illustrations were included. However serious these criticisms appear to be, the monograph contains so much fine material that these defects may be overlooked readily. If the volumes to come live up to the promise suggested in this one, it will be an unusual surgical monographic series.

Surgical Practice of the Lahey Clinic. By Frank H. Lahey. Ed. 1. Pp. 897, with 376 illustrations. Philadelphia, 1941, W. B. Saunders Company.

This monograph is constituted essentially by a series of papers published previously, the majority of which appeared in 1939 or 1940; some, however, were published as long ago as 1937 and 1938. Dr. Lahey's interest in the standardization of tech-

nique in the performance of certain operations is so well known that this volume is bound to attract the surgeon interested in thyroid, biliary, gastric, or colonic surgery. In addition, there are excellent articles reprinted on certain aspects of thoracic, gynecologic, urologic, orthopedic and neurologic surgery and anesthesia.

The volume can be recommended as representing the practices of one of the strong surgical clinics in America. Some of the papers on the colon, in the light of present practices in other surgical clinics, have more historic than current interest. One of the chief defects of such a volume is that it is incomplete; that is, many procedures of interest to the general surgeon are missing. For instance, there are no papers on appendicitis, the pancreas, the spleen, and other subjects of interest to the abdominal surgeon; these defects are even more apparent in other provinces of the general surgeon.

Pediatric Gynecology. By Goodrich C. Schauffler. Pp. 384, with 66 illustrations. Chicago, 1942, The Year Book Publishers, Inc. $5.

This unique book is the first of its kind and should be heralded by all who see the immature female for she belongs to a class of cases that often prove troublesome, with special and tactful approach being of prime importance. It presents more than gynecologic diseases but the selected abdominal surgical, urologic and proctologic diseases which must be considered in a differential diagnosis are correctly included. The medicolegal implications in sex crimes are presented and sound advice offered in a field with which the average physician is not conversant.

Much of the material included in this book has never before been published or has been widely scattered in brief communications on very narrow aspects of the subject. Few physicians ever have an opportunity to see and treat as many cases of this kind as has the author. Embryology and development of the female genitalia have been previously and adequately determined but the clinical phases are here thoroughly treated for the first time. Much of the material must be made up of the author's experience.

Worthy of particular mention are the author's recommendations for completeness in examination and exactness in bacteriologic diagnosis. Many practical procedures are given for gentleness in examination and treatment in order to obtain the cooperation of these young and easily alarmed patients. Detailed bacteriologic techniques are given, allowing the physician to proceed without further reference to other texts. Specific prescriptions are given for most infections.

The author's use of the popular but inaccurate and unscientific term "menometrorrhagia" must be condemned. Likewise, the designation of estrogenic or nonovulatory bleeding as menstruation is unfortunate. It must be pointed out that "to facilitate diagnosis" in cases with menorrhagia "curettage should be performed" not "immediately preceding an expected menstruation" but during the episode of uterine bleeding and after it has continued for at least four days. Unless this diagnostic procedure is adopted, all phases of irregular shedding of the endometrium will be missed and they should be common causes of menorrhagia at the menarche.

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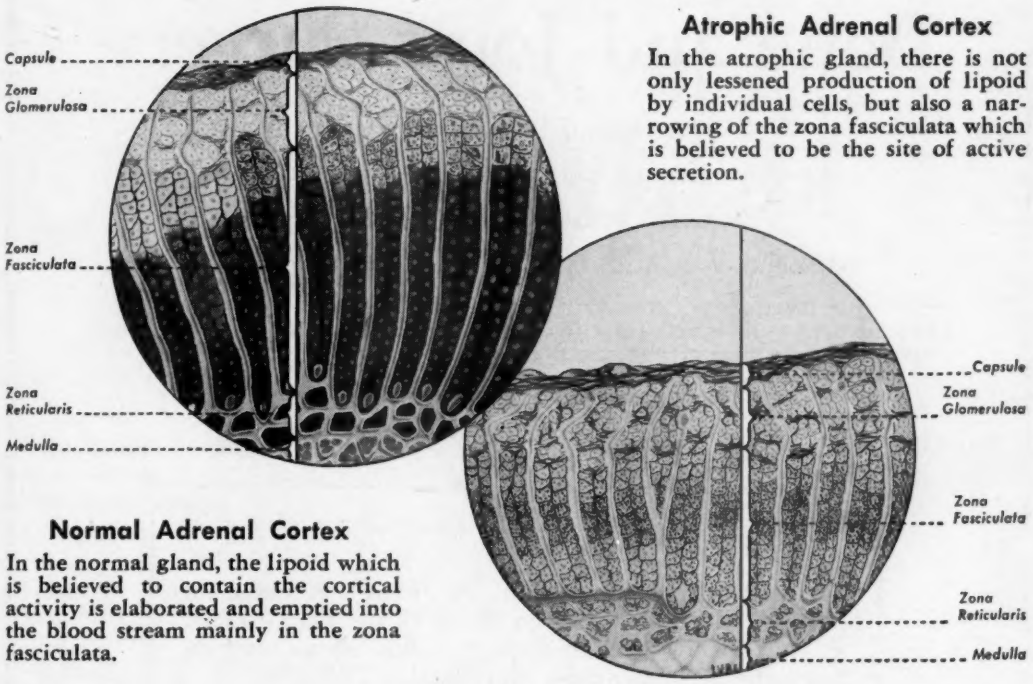

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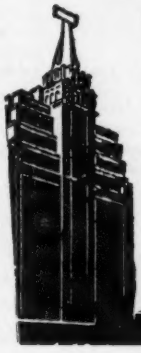

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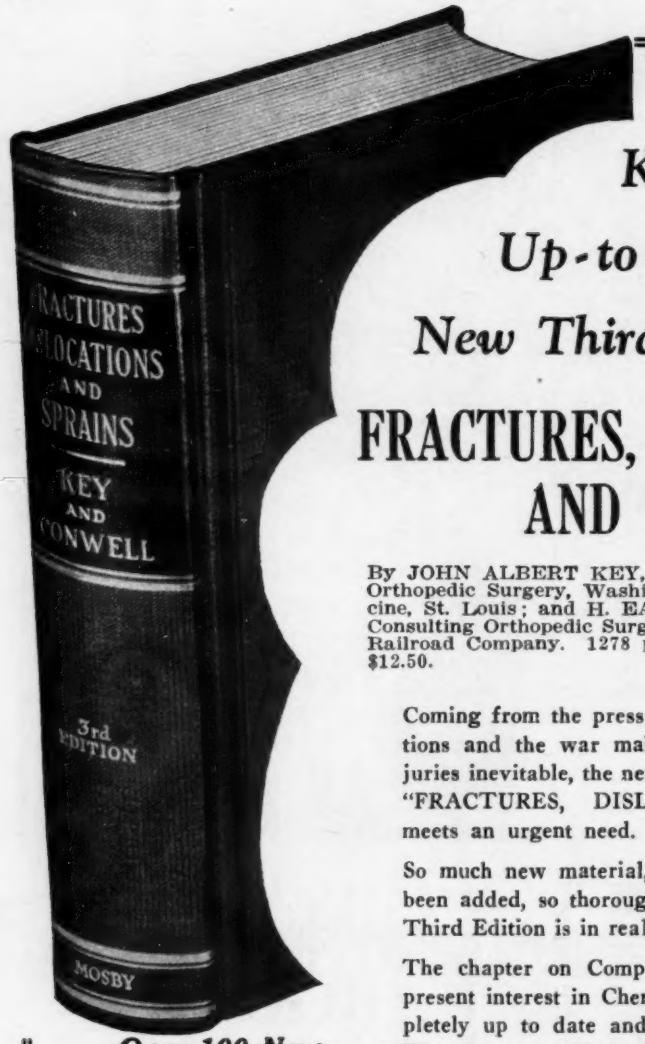

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